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The Broader Implications of Aging

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DR. COWDRY HAS DRAWN UPON HIS VAST EXPERIENCE IN THE PROBLEM OF AGING TO UNDERSCORE THE VARIABLE RATES OF AGING IN DIFFERENT INDIVIDUALS AND IN DIFFERENT TISSUES WITHIN A SINGLE INDIVIDUAL. THE URGENT NEED FOR A MORE AGGRESSIVE APPROACH TO THE PROBLEM OF AGING AT THE SCIENTIFIC AND SOCIO-ECONOMIC LEVELS CONSTITUTES THE CENTRAL THEME OF THIS PAPER. A UNIQUE PLAN FOR PRODUCTIVE UTILIZATION OF UNIVERSITY PROFESSORS PAST RETIREMENT AGE IS SUGGESTED.

OLD AGE, unlike all other hazards of life, is crushing because there is no way to avoid it. An individual may, perhaps, avoid both cancer and the atom bomb; at least, he has a fighting chance of doing so. But his only way to avoid aging is to die young. We meet cancer and the menace of the bomb with forceful action. We accept aging with regret and try to forget about it. Reports on cancer research, which is now being financed more generously, contain new and unexpected observations that make us think. Reports on research dealing with aging, starved for lack of funds, are usually a repetition of the same old facts, and promote slumber.

It does not help to be told that the best way to enjoy a long and happy life is to select parents very carefully. There is no question about it. Aging is taboo, while cancer is all the rage. Of the two, knowledge about aging and action springing from it are more needed than new facts about cancer. I admit this only after due deliberation because I am devoting the best years of my life not to the phenomena of aging but to research on cancer.

We read a lot about how happy old age can be, but somebody has said that when God figured out the processes of aging He must have been in anything but a gala mood. However, these processes are really remarkable. The ways of Nature are not simple. It is a true saying that God moves in a mysterious way His wonders to perform.

I chiefly marvel at the differences in rate of aging. Let us take two extremes. Dr. Charlotte Davenport died in St. Louis in 1936 at the reputed age of 111 years. Married three times, at the ages of 16, 18, and 69, she bore eleven sons. Shortly before her death, to the best of her knowledge, all were alive and well. The eldest was living and 93 years old. Her third marriage was to William Davenport, a man of 21 working on the *Times* in London. They lived together happily for forty years.

She traveled widely. In Tahiti she spent a month with her good friend, Robert Louis Stevenson. In England she gave lessons in physical culture to the late Queen Alexandra. She was photographed with Sarah Bernhardt. Coming to the United States, stacks of newspaper clippings, yellowed with age, bear witness to her reception by New York's Four Hundred. She was interviewed in 1889 by a young reporter on the *Marion Star*, who later became President of the United States, and

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Dr. Cowdry's address at the commencement exercises in connection with the installation of Dr. George Dinsmore Stoddard, President of the University of Illinois, May 15, 1947, Chicago, formed the basis of this paper.

whose account is available for all to read. Among her pupils was Mrs. Phoebe Randolph Hearst, mother of the famous publisher. According to society reporters, she taught Mrs. Alice Lee Longworth how to hold a cigarette properly. She was an intimate friend of Admiral and Mrs. Dewey and of Joseph Pulitzer of St. Louis.

Such activity, such endurance do not come often.

Contrast this with a young boy of about 8 years whom I saw in the St. Louis Infirmary. The victim of a rare but terrible disease, progeria, he was in effect an old man. His skin looked old and wrinkled, he was beginning to get bald, and his joints seemed to creak. The cause of this precocious aging was probably pituitary deficiency, while retarded aging in the case of Dr. Davenport was probably hereditary.

It is also interesting to consider that within a single person the processes of aging act at different speeds. The coronary artery ages much more quickly than the radial artery in the wrist. The ovary becomes senile long before other endocrines. In the disease known as Xeroderma pigmentosum, because it shows patches which are dry (Greek *Xeros*) and pigmented, a child of say 12 years has an old skin something like that of a senile at 80. Cancers sprout in it with great luxuriance, since the skin is abnormally sensitive to light, and the outcome is early death.

The life span is the limit beyond which human life, even under the most favorable conditions, does not extend. It is placed by authorities at 100 years. But the possible life span of the several systems is different from that of the whole body. As already indicated, that of the female reproductive system is short. Friedenwald gives the possible life span of the eye at 120 to 130 years if the body could last that long. Weidman speaks of the skin on the trunk of a man at 85 still affording protection as it did at 20. Epidermis, the outer layer of skin, may, indeed, have a life span exceeding that of the eye.

This brings us to the parts of the body which are veritable "fountains of youth." These occur wherever there are reservoirs of cells that never age and die except accidentally. In the bone marrow such cells exist. The life of each individual cell begins with the division of the cell preceding it and extends to the time when it, in turn, divides giving rise to two others. They are called intermitotics because their individual lives extend from the mitosis that gives them birth to the next following mitosis. To be more precise, they are classed as vegetative because they live a primitive sort of life doing little except to maintain the reservoir and to provide some offspring, which, in series, do differentiate into blood cells. Obviously those cells that tread the path of blood cell formation must be a select few, because, if all of the vegetative intermitotics did so, the reservoir would differentiate itself out of existence, and this fountain of youth would cease operations.

The most interesting fountain of youth

is in the epidermis, which continues to discharge young cells as long as the body lives. But it is not built like a fountain in the park. It is spread all over the body, within this epidermis, and the cells exuded by it take the place of the cells worn off at the surface. And epidermis is a layer of tissue, in most parts of the body of about the thickness of a thin sheet of carbon paper!

These and other fountains of youth keep playing until we die. They must be included in any broad view of aging. New and grave emergencies are arising for us and the whole world. Conversion of atomic energy from a destructive to a peaceful force requires a lively feeling of social responsibility. Education of our citizens as to what all this means is being pushed at a frantic speed by newspapers, radio, books, and speeches galore.

Our action in other emergencies which we shall have to face in the future will depend upon many factors. In the long view, it is essential to think of social action as being conditioned also by the changing composition of the nation in respect to age level and to the proportion of the sexes. A nation made differently responds differently.

An old man is not the same individual that he was in his youth. Recent investigations with chemical substances that can be traced through the body show that almost all the material of which he is composed is replaced by new material moulded in about the same shape. Even fat, which some have reason to regard as a more or less permanent handicap, is also regularly used up and replaced. Nature is a good housewife. The newly received fat is stored while that already on hand is utilized. Not the least benefit from the great advances in atomic energy, which have been so aptly described, is the use of tracer substances by which this turnover can be measured.

My point is that, though the older person is a different individual from what he once was, he has memory and can understand youth. Whereas nobody who is not aged can possibly understand how an older person thinks and feels. With age comes perspective and also tolerance, two qualities of importance in the conditioning of social action.

Because of the increase in the percentage of aged people in the nation, already an old story, we cannot be expected to respond to emergencies in the same way that we did in the time of Washington and Jefferson when we were a young nation. Looking back a short distance we find the percentage of the total population made up of people 65 years and over has steadily risen. From 1860, the decennial census year before the Civil War, to 1940 it rose from 2.7 to 6.8 per cent. It is still going up, being estimated at 7.2 per cent in 1944. Predictions are that it will reach 14.4 percent in 1980. This means that since the days of Lincoln the number of old people per hundred inhabitants has doubled and that in the expected lives of the young adults of today it will again double. The old fathers and mothers-in-law will become a real problem!

Turn now to the not so fully appreciated change in the sex ratio. In the old days the United States was not only younger in average age, it was also more masculine. There was a substantial numerical excess of males over females. The females have reduced this excess to the vanishing point at the rate of over 500,000 a decade. It was:

2,692,288 in 1910
2,092,242 in 1920
1,500,114 in 1930
453,919 in 1940

In 1944 the excess of males over females was estimated at 6,105. Today there are probably more females than males in the United States. It is a safe prediction that as the years roll by this nation will become more and more female. But, before we reach the degree of female numerical excess typical of Tibet and some other countries, we may confidently expect to be able to control the sex of our offspring.

This upsurge of the gentler sex is one of

the great events in our time. We do not know exactly why it is taking place, but there are certain advantages which females possess over males that may partly explain it. They have:

1. Greater life expectancy at all ages.

2. Greater decrease in mortality from major diseases.—Statistics of the Metropolitan Life Insurance Company for policy holders contrast the age adjusted death rates of 1921 and 1943. That for the males decreased 26 per cent while the females were far more fortunate with a 43 per cent reduction. In each of the major causes of death the females showed greater improvement. The number per 100,000 deaths is:

		1921–23	1941–43
Cancer	males	74.8	84.8
	females	88.2	82.7
Chronic heart disease	males	137.9	124.6
	females	123.0	102.7
Pneumonia	males	81.9	31.4
	females	63.9	16.1

These policy holders probably had better than average medical attention, but equal medical care for the underprivileged is extending throughout the land. If this reaping of greater advantage by females than by males from advances in medical science is shared by other millions of females, it will eventually prove a still more potent factor in the reduction of female mortality.

3. Greater privilege under the law.—The hours and conditions of labor are better for women than for men. Industrial accidents are a far less frequent cause of death. The wife gets support in divorce if she is the innocent party; whereas, the husband gets no support in the same event. The wife gets allowance in lieu of support for one year on death of her husband, but the husband gets nothing on death of his wife. In still other ways life is made easier for females than for males.

4. Less occupational shock on retirement.—Women in general are employers in the home pretty much throughout life. Theirs is a deeply ingrained employer psychology. Men are usually employers outside the home if even in a small capacity. When, in their old age, they retire to the home they suddenly must give up the employer psychology and become employees. They must take orders, not give them. Nothing like this shock is felt by the majority of women who remain dominant in the home almost to the last, yielding place somewhat reluctantly to daughters-in-law.

5. Less strain in later years owing to earlier menopause.—Thus are women early freed from the stress and strain of reproduction with the resulting consumption of energy, while men retain sexual drive many years longer. It is not by chance that the latter wear out first.

In estimating the influence on national affairs of the rising tide of females, a moment's reflection shows that more is involved than the numerical increase. Obviously we have to reckon, also, with a great increase in individual effectiveness in social action. One hundred women today are more potent in this connection than a thousand a generation ago. Thanks to the League of Women Voters, especially, this effectiveness is definitely even more on the upgrade than is the increase in number of women over men.

And there is another important point. Women are coming to hold the purse strings as never before. Many large fortunes are in their hands. It was announced not long ago that most of the stockholders in the telephone companies are women. Increasingly they have the dollars as well as the education to implement their ideas.

There can be no doubt that, in charting our course as a nation through the troublous times ahead, we shall act differently than we would have in similar circumstances in the past, because we are a different people governed by a different action system. This action system has not reached equilibrium. According to the best judgment of experts, the percentage of old people with experience, wisdom, and tolerance will increase somewhat. And, the stage is assuredly set for still greater female

influence with its kindliness and other characteristics.

Already signs can be seen of a more lively appreciation of social responsibility. The Atlantic Charter of Roosevelt and Churchill, both passed middle age, blueprinted the emancipation of the world in its four freedoms. Here in the United States, we should be the first to value the enunciation of the fine old philosopher, John Dewey, of the right of everyone to enjoy the opportunity of having socially useful experience. This I have repeatedly called the Social Magna Charta. It implies much more than appears at first sight. It fertilizes the roots of the growth of human happiness.

Briefly stated, the Social Magna Charta would proclaim the right of every individual, irrespective of age, to enjoy the experience of rendering some social service, however large or small, from advising Presidents to knitting socks. The reason people hate to think of growing old is not so much the fear of inevitable death, but rather the mental vision of years of inactivity, of uselessness, and of becoming a nuisance to their families.

The gain to be derived from a concerted effort to realize this Social Magna Charta is twofold. There is the advantage to the nation and to the individual.

First, throughout the land the movement to force people into early retirement is gaining momentum. In the professions the age now is about 65. In nonskilled industry it is lower, usually by reason of decreased manual dexterity, strength, and endurance. Consequently, an increasing fraction of the population is being thrown into the discard. This is uneconomical, to say the least. To give to these outcasts the opportunity to enjoy the experience of rendering some service of use to others is difficult. It cannot be done by a wave of the wand. The trouble is that individuality increases with age. Great diversities appear in the possibilities of service. No wholesale method will work.

Old folks are something like the variety of fish in tropical waters, all mixed up together and therefore of little practical value. The fish in Northern seas are less diversified, and tons of one kind, and of about the same size, can be caught so that Northern fisheries have great economic value. Our young adults are likewise of great service, easily mobilized, because hundreds of thousands can do the same thing in mass production. To utilize, as we must, the rapidly increasing number of people being wastefully retired involves the great task of estimating the social value of each individual and of placement so that the value can be realized.

Second, consider the benefit to the individual of being in some measure useful. The shock of retirement would be lessened. Indeed it would be a logical step not to retire suddenly on, say, July first, but progressively at the rate of perhaps 25 per cent in each of four years, gradually assuming other duties that the individual is better able to perform. The result would be a happier, longer, and more productive life.

We like to think of the universities as the leaders in civilization. They have brought the atomic bomb with its problems. They should also be the first to live up to this Social Magna Charta.

At present it must be admitted that numerous professors, as well as others, are forced into retirment although they are able to continue some sort of useful service. These individuals not infrequently find it difficult to make ends meet; for the contributing annuity plan by which both they and the university set aside a certain percentage of salary has not been in operation long enough to provide for the necessities of life. They face two handicaps, nothing to do and lack of money. And they soon go to pieces. A few universities do pay adequate pensions. But I have yet to hear of one which has special machinery set up and in operation adequately to serve its staff in this major adjustment.

I hope to see some university establish a Retirement Department and implement it with a suitable budget. It would be the

duty of this department to offer confidential counselling service to members of the staff about to retire. This, I am sure, would be welcome. The purpose would be to organize and gently to supervise activities after retirement which would benefit both the university and these individuals throughout the remainder of their lives.

Many activities of this sort leap to the mind—continuation of research, a little teaching, occasional service on committees, travel as a university representative, gathering of data and writing of reports helpful to the administration of the university or to its staff, proof reading, and so on. The essential thing is to give the opportunity to enjoy the health-giving experience of rendering some service to the university or through the university to mankind, to hold them as respected members of the team. The gain to the university would be substantial in actual accomplishment, and morale would improve, not only of the older members of the staff but also of the younger ones, who would see what is in store for them.

Thus, the initiative should be taken by some leading university in realization of the Social Magna Charta in its own ranks from which it might well spread near and far. The whole nation would then be better able to advance, overcoming one emergency after another.

SUMMARY

The status of the general problem of aging is discussed, and the need for more active support for research in aging is stressed. Cases of extreme longevity and progeria are cited; the variable rates of aging in diverse body tissues are contrasted.

The number of old people in this nation's population is steadily increasing, while the relative number of females is increasing disproportionately to the number of males. The advantageous position with respect to longevity of the female in present day society is considered, and the need for greater social and economic utilization of our old population is emphasized.

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Factors Contributing to Mental Disease in the Aged

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THE MENTAL CHANGES WHICH OCCUR WITH AGING PLAY A ROLE IN THE CAUSATION OF MENTAL DISEASE IN LATER LIFE. DR. STIEGLITZ DISCUSSES 1) THE CHANGES—PHYSICAL, MENTAL, AND EMOTIONAL—WHICH OCCUR WITH AGE, 2) THE PHYSICAL DISORDERS OF LATER YEARS WHICH ARE FACTORS IN THE CAUSATION OF MENTAL DISEASES, AND 3) THE ETIOLOGIC FACTORS WHICH APPEAR IN THE BACKGROUND OF MENTAL ILLNESS IN THE AGED. EMPHASIS IS PLACED ON EARLY DIAGNOSIS AND TREATMENT OF THE PATIENT AND NOT MERELY THE SYMPTOMS OF THE DISEASE.

AN UNDERSTANDING of causation is of the greatest importance in all phases of medicine. Diagnosis should be far more than merely applying a label to a clinical state. The primary purpose of diagnosis is to guide treatment.

Differentiation of pathologic entities alone does not suffice, although it may be academically interesting. Too often has there been greater concern with the identification of a disease than with the patient who has the disorder. This unfortunate attitude is rather bitterly expressed by the still too popular phrase, "The operation was a success but the patient died." If diagnosis is to be fully effective in guiding treatment, it must include consideration of the causation of the disease.

Furthermore, there should be evaluation of severity of disease state and some estimation of the probable rate of progression. Perhaps instead of using the dictionary definitions of diagnosis as the art of distinguishing one disease from another we would do better to consider diagnosis as a critical analysis of health of an individual conducted for the purpose of guiding therapy and prognostication.

If we follow the broader analytic meaning of diagnosis, we can see that it must include four significant aspects (14):

1. Identification of the disease state,
2. Determination of the etiology and pathogenesis of the disorder,
3. Measurement of the severity of the disturbance, in terms of functional impairment of the structures primarily involved, the degree of disablement of the individual as a whole, and
4. Estimation of the rate of progression of the disease state.

Phrased more simply, we can say we need to know what it is, why it is, how severe it is, and how fast is it changing. Diagnosis is always an opinion and is therefore open to revision.

Certainly all forms of therapy are tremendously handicapped when we attempt to operate in ignorance of cause. Truly effective prevention and cure are both predicated upon the removal of all major etiologic influences.

Some diseases occur at any age; others are much more frequent in the later years of life. The most significant of the somatic disorders common and characteristic in later maturity are included under three major groups: circulatory diseases (which include arteriosclerosis and hypertensive disease with its many variable sequelae), metabolic disorders (such as diabetes mellitus, anemia, malnutrition, the climacterics and gout), and benign and malignant tumors. These are mentioned because they are so closely related to the more common mental diseases in later years.

The three mental diseases in the aged which I intend to consider here are: arterio-

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A lecture delivered in a post-graduate course in psychiatry, George Washington University School of Medicine and St. Elizabeths Hospital, Washington, D. C., February 26, 1947, formed the basis of this paper.

sclerotic dementia, senile dementia, and involutional melancholia (8). It should be emphasized that all three of these are psychiatric expressions of systemic disorders and that in considering their causation we have to study the pathogenesis of somatic change and the functional alterations induced by the systemic phenomena.

The complex problem of the etiologic diagnosis of these chronic and progressive disorders is easier to comprehend if we break down the broad question into three subdivisions and consider each of these consecutively. First, we need to know something of the peculiarities of the patients in which these disorders arise. Second, the so-called degenerative diseases present certain characteristics which generically affect their etiology. And third, the mechanisms of causation itself are amenable to analysis.

The Older Patient

Let us consider first some of the characteristics of the older individual as a biologic organism (16). I cannot refrain from emphasizing that to age is to change and that the changes of aging are continuous, gradual, and insidious. There is no sharp line demarking the phases of the life span or specific age at which individuals become old. Aging starts with conception and continues until death. We have slipped into a careless habit of making rather arbitrary distinctions between the child and the adolescent, the young adult and the senescent, and the senescent and senile. As aging is part of living, and is but the inevitable consequence of duration, everyone ages unless they die young. The rate of aging is extremely variable. Biologic and chronologic time are by no means identical. Age should not be measured in chronologic years.

The changes of senility may be observed in very young individuals. On the other hand, there are some persons who accumulate an imposing chronologic age but remain biologically young. This asymmetry of the rate of change with age is of the greatest clinical importance. Not only do different individuals age at different rates, but within the same individual age changes vary considerably in different structures and functions. The rate of aging is not constant through the life span. Aging becomes slower and slower. There can be no hope that even in the future the measurement of biologic age can be based upon any single or simple criterion. We are not of the same function or structural age throughout. The mensuration of biologic age is as yet largely a question of applying that vague but valuable instrument known as clinical judgment.

Considerable progress has been made in the last few years, both in the direction of somatic functional testing and in the field of psychometrics, where batteries of tests give us some indication of intellectual maturity. Precise methods for measuring emotional maturity must wait until psychiatrists can agree on what emotional maturity really is. It is essential to keep in mind that mere chronologic time does

not determine how old an individual is in the biologic sense.

As previously stated, to age is to change. Therefore, the aging or aged individual is a different person than he was in his youth. There is a parallelism between the attitudes of modern pediatrics and those of geriatrics. Pediatric medicine made little advance until it was realized that the child is something different than merely "a little man." When it was finally appreciated that infantile and juvenile nutrition, anatomy, physiology, immunity, intelligence, and emotional equilibrium are peculiar to the age, pediatrics made impressive and rapid strides (15). Precisely similar attitudes should apply when we are dealing with the other end of the life span. The aged should not be considered as identical or even closely similar to individuals in middle life, merely chronologically older.

The changes which come with age are not due solely to the passage of time. In addition to undergoing what we might call pure aging, we accumulate the consequences of innumerable insults. The greater the age, the greater the accumulation and the more significant the consequent scars and depreciations become. In every life there occurs repeated infections, intoxications, fatigues, psychic and physical traumas which in summation constitute the unavoidable vicissitudes of existence.

These detrimental experiences are part of living, for existence in a sterile and completely sheltered environment can hardly be called life. In a sense they are desirable and necessary despite the accumulating detriment. Life is a kinetic phenomenon and stresses and conflicts serve as stimuli encouraging growth and vigor in all structures and functions. For example, it is doubtful whether an infant fed from birth on nothing but purified amino acids, fats and glucose, with suitable vitamins and minerals, would ever develop sufficient gastric glands to be able to enjoy and digest a steak in later years.

Certainly struggle is a necessary element in the development of the mind. Defense mechanisms do not become vigorous in the absence of need for defense. Such is the philosophy behind all active immunization. All living things are encouraged to develop by use; disuse engenders atrophy.

It is therefore academic rather than pragmatic to try to distinguish the consequences of pure aging from the scars of the many minor and major injuries which are inevitable in social living. Among the pathologists particularly interested in the structural changes of senescence and senility there is no agreement as to what is due to aging per se and what to the scarring of disease (7).

With this in mind, it is not difficult to understand that there can be no sharp line of division between the normal and abnormal. Health is relative and we cannot say that "A" is perfectly well and "B" diseased. "A" is merely less sick than "B." Obviously the degree of health is related to biologic age. This viewpoint may be novel to those who are still indoctrinated with the old definition of health. Even the later editions of medical dictionaries define health as that state of being existing in the absence of disease and by this definition imply rather abrupt transition.

Health is in truth an ideal abstraction and perfection in health is probably unattainable (15). If we redefine health as that state of being in which all the reserve capacities of the organism are at their maximum, we see at once that there must always be room for improvement in healthfulness. The degree of our health parallels our effectiveness in living. Similarly, disability from disease or loss of health causes an individual to be increasingly ineffective in living. Senescence alters our biologic efficiency in many ways.

What are the changes which are consequent to senescence and which are significant to the problem before us? Many changes of age are so obvious that it is ridiculous to consider them here, particularly since the most conspicuous changes, such as wrinkles, presbyopia, graying hair, or baldness are the least consequential. It

really makes very little difference whether the roof be covered with a thick thatch or be a gilded dome. What is important is what goes on underneath this roof.

Much more important are many subtle, and insidious, biochemical and metabolic alterations which are occurring in all of us. There is still much to be learned about these obscure variations in life processes, but what is already known points the way to increasingly important discoveries. It should be stressed that because these changes are subtle, gradual, and insidious, they are usually ignored until so far advanced that they become obvious. At that time they are irreversible.

For example, most of us are prone to be misled by the fact that the more obvious effects of arteriosclerosis are rarely observed before the meridian of forty years. Actually, the arteriosclerotic processes began many years before this, but our methods of detection are crude and there is little effort exerted in the direction of earlier clinical discovery. These subtle changes must be assiduously searched for if we hope to learn anything about their early pathogenesis.

The structural or anatomical changes of aging arise from variations in the relative emphasis of two processes which go on simultaneously throughout life: atrophy and growth. In youth, growth predominates although there are many illustrations of the atrophic process, even in the embryo. The processes bringing about disappearance of the rudimentary gill clefts and the atrophy of the ductus arteriosus are similar to the tissue atrophies of senility.

In later years, as growth is slowed below the replacement level, there is in sum total a shrinkage of mass. Atrophy is much more marked in parenchymal tissues than in the mesenchymal supportive elements. As a result, the proportion of collagenic connective tissue to parenchyma is altered (7). Thus we see fibrosis arising gradually. This is the most typical structural change which occurs with aging.

But fibrosis, whether it be in aging arteries, in the arteriolar walls of hypertensive disease, in old kidneys, or in a cirrhotic liver, is not an aggressive process in which collagenic tissue invades, pushes aside, and destroys parenchymal cells. It appears rather as a protective phenomenon, wherein the simpler and more primitive connective tissue grows to replace the already atrophic parenchyma. Despite the reiteration, it should be emphasized that this gradual atrophy of parenchyma with fibrotic scarring is a very gradual phenomenon which begins so silently that it is rarely discovered until years after the changes have begun.

What about the parenchymal atrophy? Why does it happen with aging even in the absence of gross or detectable injuries? Is it because the cells themselves have become old or is it because of some change in the environment of the cells? The answers to these questions are not yet settled, but the evidence points more and more to the concept that the primary depreciations arise in the environment of the parenchymal cells.

In the first place, only a very few of the cells of our bodies are as old as we are. With the notable exception of the cells of the central nervous system, all other functioning elements are constantly replaced. Therefore, the older individual is not made up of particularly old cells.

Furthermore the epochal discoveries of Carrell have demonstrated convincingly that grown in a proper medium, tissue cells are practically immortal. The tissue culture of fibroblasts in his classical experiment survived with unabatable vigor and with no detectable depreciation of vigorous growth for over thirty-four years, or about four times the maximum known life span of the chicken. The experiment was terminated only last year because there seemed to be no valid reason for its further continuance. However, this apparent immortality would have been impossible were not the media in which these cells grew not only ideal to start with, but refreshed every forty-eight hours over all these years.

Permit tissue culture media to remain unchanged longer than this and the failing supply of nutriment and the accumulating metabolic debris soon destroys the culture.

Thus it is in the internal environment of the tissues, the spaces between the tissue cells, that we must search for the reasons for the depreciations of aging. The life and vigor of all cells are dependent on the maintenance of a nearly constant optimum internal environment. Unquestionably the earliest alterations which occur are too minute to be detected and involve the tissue enzymes, co-enzymes, and catalists (17).

The later appearing phenomenon of fibrosis adds to the difficulties of parenchymal nutrition. The transfer of nutriments, including oxygen, and the removal of the metabolic debris are impeded by the fact that vascular walls are thickened and the intercellular spaces contain more collagen. It is notable and significant that the depreciations of aging and of the so-called degenerative, or slowly progressive diseases in later years, have essentially the same effects upon tissue nutrition.

Functional activities are affected chiefly by depreciation of the effectiveness of homeostatic mechanisms. Those many, and often elaborate, mechanisms which are essential for the maintenance of equilibrium in the internal environment become slower in their response and less vigorous in compensating for external forces which tend to upset balance.

In addition to this quantitative depreciation, there are also certain qualitative changes in homeostatic responses. The absolute necessity of maintaining the internal environment within very narrow ranges is familiar to all. Many of these ranges have been pretty well defined by extensive studies. They are spoken of, in a loose way, as physiologic constants, though they are not precisely constant. It is notable that such examples as body temperature, blood content of chloride, sugar, calcium, urea, and the like remain practically the same throughout life, with the single and interesting exception of the metabolic rate.

Though the internal environment, as measured by simpler analyses, remains much the same throughout the span of life, the ability to maintain it depreciates after maturity. For example, older individuals show definite change in their response to the glucose tolerance test; the sugar content of the blood rises to higher levels than in youth and falls more slowly. The curve as elicited in the aged resembles, but by no means parallels, that of younger diabetics.

Secondly, older individuals cannot tolerate extremes of temperature. Atrophy of sweat glands and reduced ability to dilate the cutaneous blood vessels impairs adaptation to hot environmental conditions. The lower metabolism and greater rigidity of the vessels interfere with heat conservation in the aged, thus impeding adaptation to cold. Water balance in the aged is less stable than in young adults. In this respect the senile resemble infants.

The clinical consequences of the slowing of the vital homeostatic mechanisms are very important to all of us. In the first place, the symptoms of disease are much less conspicuous in later years. Most of the clinical phenomena which are indicative of disease arise as responses to factors disturbing equilibrium. Fever is one such, and the aged may suffer from severe infections, such as pneumonia, with negligible rise in the body temperature. Here is at least one factor which contributes to the asymptomatic and insidious nature of disease in later years.

Furthermore, repair after injury is slower, and, as a result, convalescence takes longer. The response to medication is affected, and ill effects of an accumulation of drugs must ever be guarded against. Even such simple but often abused items as baking soda can lead to a severe alkalosis because the ability of the body to cope with the extra alkali is impaired.

It must be remembered that functional

reserves go through long and silent periods of depreciation before the impairments are clinically conspicuous. We start out life with immense reserve capacities to handle extra stresses and strains. With aging these are gradually nibbled away until in one or more functions the capacity falls below physiologic demands. Then, and only then, do the symptoms of functional failure appear. Therefore, depreciation of reserves is entirely symptomless unless the function be subjected to unusual stress.

For example, the young mammal starts out life with about four times the renal functional capacity that is necessary to get rid of normal metabolic debris. In the course of a lifetime this margin of safety is gradually reduced both by the wear and tear of normal living and by the accumulative effects of many intoxications and infections.

An acute nephritis may depress functional capacity below requirements; the picture of renal decompensation appears. Following recovery from the acute stage, functional efficiency does not go back to its previous level. Some of the damage is residual and permanent, although no evidence of kidney failure is elicited, and routine urine analysis may reveal no abnormalities. However, the margin of safety is lessened. Later, additional insults may depress capacity to a point below the required physiologic work load and terminal renal decompensation, or uremia, supervenes.

Similarly, silent depreciation of the cardiac reserves is so common that it can be assumed. A parallel situation also occurs in the capacity to withstand emotional trauma. Harold Palmer (9), in an analysis of involutional melancholia, emphasizes the uniformity with such characteristics as a constricted horizon, sadism or masochism, a repressive note as regards pleasures, and a tendency toward perfectionism are notable many years before the appearance of the frank psychoses. Compensatory processes become exhausted until finally a relatively minor trauma may suffice to precipitate a disabling melancholia. The significant thing is that the margin of safety or tolerance to emotional trauma is already reduced.

Though depreciation of these various reserves are without subjective or objective symptoms, they are not undetectable when the trouble is taken to search for them. Such depletions can be revealed by the creation of suitable conditions of stress, in which a specific functional burden is deliberately increased. To illustrate, the only really effective way of determining the reserve of an automobile motor is to drive the car up a steep hill. Its behavior on a level road or while idling at the curb may be most misleading. The more valuable physiologic stress tests include the glucose tolerance test, the renal concentration test of Fishberg, and the like. There is great need for the development of more such procedures for measuring the reserves of other functions if truly comprehensive measurements of health are ever going to be made.

The mental changes which occur with normal aging play a role in the causation of mental disease in later life. It has been frequently commented that one of the characteristics of senile dementia is diminishing contact with the environment (4). In part this is unquestionably related to poorer preception of the environment (6). Vision becomes somewhat dimmed and the presbyopic eye loses power to accommodate for near vision; hearing is often impaired and senses of smell and touch become less acute. Failure then to remain in active contact with the environment is not solely central. These handicaps in the machinery of perception must not be ignored.

With aging, memory gradually becomes poorer, particularly for recent events. This is normal but greatly exaggerated in arteriosclerosis or in senile patients (11). Reduction in memory is not all organic or due to true functional depreciation. My own observations have led me to the conviction that much of the failure is due to inattentiveness because the more mature per-

son is not particularly interested in remembering such items as names and telephone numbers. At the time the information is first received, if interest is lacking, it will make only a very superficial and transient impression. Exaggeration of this trend does, of course, contribute to mental incompetency.

It is characteristic that the normal and perfectly vigorous older mind becomes less concerned with the present and more and more interested in correlating the past with the future. The small child lives only for the moment; the mature individual finds the present moment but a fragment of his experiences and gives it relatively little attention. For example, the definition of "today" as being merely "yesterday shaking hands with tomorrow" could have been given only by a mature person (16). This characteristic must be kept in mind in evaluating mental attitudes in later maturity.

Much has been said and written regarding changes in the ability to learn with advancing years (5, 16). The most accurate and comprehensive psychologic studies made thus far indicate that depreciation is extremely slow if the function of learning is continued (6). Disuse accounts for more of the decline than aging per se. The ability to learn is tremendously affected by motivation. If curiosity is a powerful characteristic, learning continues throughout life. Observations of Doctor Carl Camp (1) indicate that older persons given a paragraph to memorize will take longer than young persons but will make fewer errors because they are less sure of themselves and go over it again and again to be more certain that they have it correct.

The emotional changes which occur with normal aging are far too complex to consider here. Emotional maturation does not parallel intellectual development; often it is arrested at a relatively early stage and we have an individual intellectually mature but emotionally juvenile. It is my opinion that these are the individuals who, if they live long enough, ultimately go into what is called the second childhood. I personally doubt that there is such a thing as *second* childhood; it is probably merely a continuation of the first original immaturity which has been concealed during adult life by conventionality of behavior. These characteristics of immaturity reappear in senility because it becomes increasingly unimportant to make an impression upon others and thus the need of continuing conventionality disappears.

Much has been said in the past of increasing narrowness of interest and rigidity of the older individual (2). That these characteristics do appear with increasing prominence is unquestioned, but the reasons are open to several interpretations. It is my feeling that much of the rigidity is a result of habits. Habits, both mental and physical, good or bad, are created by repetition over a period of time. Thus, time is a factor in the development of habit patterns and the older the person, the longer the duration of repetition.

It is not surprising, therefore, that with aging, mental habits become more and more fixed, and that a certain rigidity of temperament and increasing narrowness of interest would follow. We can say that the leopard does not change his spots with age, they merely become intensified. This is true of personality characteristics of all sorts: the understanding thinker becomes increasingly tolerant and wise with the passage of time, but the sanctimonious become intolerably opinionated bigots. The young fool becomes the old fool unless he bless the community by dying young.

Disorders of Later Years

So much for the factors inherent in the aging individual. Physical disorders common in later years have certain characteristics which have significant implications in the causation of mental diseases in this part of life. Many diseases occur at any age, although the reaction of the individual to the disorder will vary. However, the so-called degenerative disorders, which we prefer to call the chronic progressive dis-

eases of later years, become increasingly frequent in later maturity and their coexistent presence very definitely contributes to mental disease. These disorders include three related major groups:

1. Circulatory Disorders:

Arteriosclerosis
- coronary → heart disease
- cerebral → arteriosclerotic dementia
- → apoplexy
- pancreatic → diabetes mellitus
- renal → chronic nephrosclerosis
- peripheral → Buerger's disease

Hypertensive arteriolar disease
- Similar consequences, depending upon the distribution and abruptness of most extensive arteriolar constriction

2. Metabolic Disorders:

Malnutrition
- anemia
- myocardial damage
- cerebral damage (senile dementia) (18)

Anemia
Climacterics
Diabetes Mellitus
Gout

3. Neoplastic Disorders: Cancers

All of these disorders have certain characteristics in common which throw them in sharp contrast to illness encountered in youth. Perhaps one of the best ways of defining their characteristics is to point out their differences (14):

Four of these characteristics are particularly important. First, the silent insidious asymptomatic onsets are significant. Because there are no subjective evidences of anything being wrong, these disorders are rarely discovered until progression is so advanced that structural alterations become irreversible. This means that there is little opportunity to observe the pathogenesis of these disorders at the time when causative influences should be most readily discovered. Treatment is instituted late, and etiology is even more obscure than it really needs to be.

Second, the multiplicity of etiologic factors is of the greatest importance. All of these illnesses arise as a result of a series of accumulated and superimposed insults, and the nature of these insults and their sequence is not necessarily the same in any two cases. The obscurity of causation, as has been mentioned previously, greatly handicaps the development of comprehensive and scientific therapy, both preventive and curative.

Third, the overlapping nature of all of these disorders must never be forgotten. Rarely do we see an elderly person with but a single chronic progressive impairment. There has been too much refinement in attempting to separate some of these processes into artificially delineated entities.

The physician dealing with the sick

Disease in:

Youth			*Senescence*
Etiology:	Exogenous Obvious Specific (single) Recent		Etiology: Endogenous Occult Cumulative Multiple (superimposed) Often past
Onset:	Florid	—VS—	Onset: Insidious; asymptomatic
Course:	Acute Self-limited Immunizing		Course: Chronic Progressive (long disability prior to death) Not protective (increase vulnerability to other diseases)
Little individual variation			Great individual variation

child has a right to assume that the child has only one disease and that the patient was probably in reasonably good health prior to the acute disorder. He can therefore presuppose with considerable degree of safety that all clinical symptoms and signs presented are associated with and attributable to the one disease. When, however, the physician is faced with problems of diagnosis in the senescent individual, he must reverse his attitude and presume the presence of several superimposed impairments. If the illness be an acute one, he is faced with the question of deciding which of the clinical phenomena are due to new and acute disorders and what is secondary to pre-existing disturbances. Such disorders as diabetes, arteriosclerosis, hypertensive disease, and the like commonly co-exist.

Fourth in significance is that they all have a common denominator in the fact that they interfere with nutrition of the parenchymal cells because of changes in the inter-cellular matrix. Any interference with the internal milieu impairs the vigor and functional capacity of the parenchyma. These disorders may impair tissue vitality by any one or more of four factors (16):

1. Inadequate nutritional supply (dietary deficiency, avitaminosis, anemia, etc.),
2. Inefficient distribution (circulatory impairment, etc.),
3. Ineffective utilization (insulin deficiency, etc.), and
4. Accumulation of injurious metabolic debris (renal inadequacy, etc.).

The clinical consequences of circulatory disease can be and frequently are most varied despite the relative uniformity of the underlying processes. Determinants are: the abruptness or gradualness with which parenchymal histanoxia arises, and variation in the intensity of the lesions of arteriosclerosis and arteriolarsclerosis in different areas of the body. Gradual narrowing of the coronary vessels creates the state of relative coronary insufficiency; abrupt closure by thrombosis causes myocardial infarction (10). Similarly, prolonged but moderate cerebral malcirculation is typical of arteriosclerotic dementia; sudden blockage of circulation by either hemorrhage or thrombosis leads to apoplexy.

We are still totally unable to explain why arteriosclerosis in one individual affects the cerebral vessels more severely than other arteries, thus resulting in arteriosclerotic dementia, and in another involves the coronary vessels primarily, or in still another the pancreatic vessels, inducing diabetes, or in a fourth the arteries of the extremities with resultant claudication, or in a fifth the renal vessels with renal decompensation as the terminal event.

The complex riddle of arteriosclerosis will not be fully solved until the reasons for this variability in distribution are explained, as well as the reasons for the pathologic changes in the blood vessels themselves (13). The individual variations in the distribution and intensity of the lesions of arteriosclerosis emphasize the importance of individualization in diagnostic study of senescent individuals.

Etiology

The evolution of etiologic thought, like other evolutions, has been a long, slow, and often painful process. Primitive man, requiring some explanation for mysterious aches and weaknesses, sought solace in placing the blame on supernatural influences. This absolved him of responsibility for his own illness. Demonology, and later, Divine Wrath had their vogue as men shifted more and more responsibility from themselves onto God.

Later came dim awareness of the relation of epidemics to certain environmental factors and the appearance of many vague theories of miasmata, vapors, and humors. Although there were glimmerings of the concept of contagion during the terrible epidemics of the Dark Ages, modern etiologic thought began with the epochal

discoveries of Pasteur, and the birth of the new science, bacteriology.

Pasteur's discovery that certain diseases were due to invasion by microorganisms or bacteria was quickly followed by Koch's equally significant studies concerning the specificity of the organisms responsible for specific disease entities. The postulates of Koch became the basic law of the new science. Feverish research, spurred by the hope that in this vast realm of pathogenic bacteria would be found the explanation of all disease, led to many brilliant and invaluable discoveries. One after another, the specific organisms of infective diseases were identified, isolated, and studied. The science of immunology developed as a collateral branch. Diphtheria, typhoid fever, the dread summer complaint of infants, plague, cholera, and several other diseases were quickly controlled, once their infective origin was known.

But the dreams and hopes of the earlier bacteriologists have not materialized. Invading microorganisms do not cause all disease, and even when they are involved, they are not the sole cause of infective diseases. The concept of specificity, though invaluable in preventing many hasty and erroneous conclusions, also blinded many scientists and retarded etiologic thinking.

The idea of specific causation is not yet dead; a new menace has been discovered in nutritional deficiencies and there are those who now wish to attribute almost every human ill to nutritional defects. They too are doomed to fail, though from their failure much good will come, for certainly defective nutrition contributes to the causation of many ills. Science is vulnerable to fads and fashions. We must be constantly on our guard not to be carried away by fashionable enthusiasms.

Causation is always a combination of multiple factors. Nothing happens from just a single cause. This is as true of wars, marriage, explosions, floods, or earthquakes, as it is of disease. It would be immensely beneficial to all thinking if the singular of the word cause were deleted from vocabularies, and the more flexible term causative factors used in its place.

Causative influences are amenable to analysis. They fall under three categories: predisposing factors, provoking factors, and perpetuating factors. These three types of influences are invariably present in the causation of any and all illness, although they are not necessarily of equal importance. Disease is comparable to the long-famous illustration of the camel's spinal fracture; it was not just the last straw that broke the back of this unfortunate beast of burden, but this last whisp of cellulose *plus* all the previous loads, which may not have been straw at all, but hay, or figs, or bricks, or harem ladies, or kegs of wine! And in no two instances are these predisposing factors necessarily identical.

Although all three of the categories of causative factors are invariably involved, they are not necessarily of the same relative importance. Therefore, a truly effective etiologic analysis (which should be included in every diagnosis, even though it be but an opinion or impression) should make some effort to evaluate the relative weight of the various factors.

Such an impression added to the diagnosis (which unfortunately is usually limited to giving the state of ill health a name) should add immeasurably to prognostic and therapeutic competence. For example, it is known there are hereditary factors in the causation of cancer. These predisposing influences may or may not be particularly notable in a given instance. In cancer of the bladder due to aniline, the provoking irritant is the most important, for these tumors many times arise in individuals who have no family history of cancer whatever. With this in mind, one is far better able to answer the inevitable question as to the probability of cancer in succeeding generations, and thus add greatly to the peace of mind of many people.

Clearly, in any acute disorder, the predisposing and provoking factors must add up to 100 per cent in order to induce the illness. Their relative weight can be a

valuable indication of the probable outcome. Supposing we have two instances of an acute and disabling anxiety state. In one patient it was induced by relatively trivial emotional trauma, in the other a profound shock proceeded the appearance of the psychosis. Obviously, in the first instance vulnerability (predisposition) is high, because the provoking insult was trivial. Recurrences are probable. In the second instance the likelihood of recurrences is very much less. I would urge you therefore to include some impression of the relative force of predisposing, provoking, and perpetuating influences in etiologic analyses, even though it be only a tentative impression. The development of such a habit is useful.

Among the more common etiologic factors which appear in the background of mental illness in the aged, both predisposing and provoking influences conditions which effect cerebral nutrition or cause cerebral intoxication, as well as more remote emotional factors have to be considered. Whether these will be predisposing or provoking will depend to a great degree upon whether they are slowly accumulative or abrupt and intense.

For example, cerebral histanoxia or inadequate oxygenation of the cortical tissues is a most important factor. This may be chronic as a result of arteriosclerosis or hypertensive disease, especially if complicated with moderate anemia, or it may be acute as a result of sudden fluctuations in blood pressure. A relatively rapid fall of hemoglobin content of the blood from any cause may be the provoking element. The acute psychotic disturbance seen in hypertensive disease as a result of relative hypotension (12), which may be due to transient cardiac incompetence, surgery, or to overrapid and overenergetic medication, closely resembles the agitated periods of arteriosclerotic and senile psychoses.

Vitamin deficiency plays a role in depreciation of the brain (18). This is much more common in older individuals than in youth because depletion with a mildly inadequate intake involves duration. Hormonal imbalance, such as may occur at the climacteric or with the depressed metabolism of hypothyroidism, can make the brain very much more vulnerable to other sources of injury and thus act as predisposing influences.

Intoxications likewise may be acute or of long duration. Fatigue should be considered among the intoxications. The abuse of alcohol over many years plays a role. Mild subclinical plumbism is much more common than is usually realized; it is rarely discovered without specific search. Every infection is a source of toxic injury, and the so-called cloudy swelling of fever, no matter what its origin, presumably always leave some residuum of damage. Metabolic intoxications such as occur in the azotemia of renal failure, extreme hyper- or hypo-glycemia, or the toxic debris in intracranial edema may be either predisposing, provoking, or perpetuating sources of damage.

The intoxication which occurs premenstrually in young women and is frequently associated with great changes in mood (either depression or excitation) is associated with change in water balance and the psychiatric phenomena respond extraordinarily well to diuretic medication with enteric ammonium nitrate. Here we have an illustration of therapy directed against cause rather than against symptoms. That there are other and as yet unknown sources of intoxication is certain.

Social and economic factors which contribute to the rapidly increasing number of senile patients in hospitals for the mentally sick must not be ignored (3). The numerical increase of the elderly in the population is greater than most physicians realize. In the decade from 1930 to 1940 the total population of the United States increased 7.2 per cent, but the increase of those aged 65 or more was 35 per cent, or nearly five times the relative rate of increase.

Secondly, migration from rural to urban areas, with the greater complexity of city life, puts many old people in the category

of being incompetent to continue free in society. The mildly confused, poorly oriented, slightly noisy, and careless old man can be kept useful in the household on the farm for many years. He is, however, impossibly inadequate as a member of a family living in a kitchenette apartment.

Society's attitude toward the mentally handicapped is changing; there is much less disgrace in institutional care, and society has been encouraged, especially over the last fifteen years, to pass their responsibilities over to a paternalistic state. Employment difficulties and the threat of enforced retirement are not infrequently the precipitating factors which lead to the necessity of institutional care.

Compulsory retirement, either because of age or purely physical disability, usually means a great retraction in the standard of living in spite of social security benefits. Abrupt decline in standards of living is often such a tragedy that the older individual breaks down. A survey made in New York State in 1929, which you will note was before the depression, revealed that of people aged 65, only 5 per cent were able to continue living at or near their previous standards; 28 per cent continued employment, and 67 per cent were dependent upon either family or state for support. The chances of saving in the future are even less. The war must be paid for.

Insecurity in relation to employment may not be solely financial. There is great emotional tension inherent in the conviction that one has been inadequately promoted and that younger men are being advanced. Excessive promotion, beyond the capacity of the individual to assume the greater responsibility, may be the last straw.

Anniversaries encourage stock-taking and can thus precipitate profound depressions. Boredom upon retirement has contributed to the premature death of many despite the fact that it is predictable and preventable (16). Loneliness, due to increasing isolation in the family and the gradual shrinking away of a circle of friends through death, is another contributing emotional factor.

The climacteric and the chemical changes which occur with it has been blamed for much in which this phenomenon is in no way responsible. Even in involutional melancholia, which is more intimately associated with sexual involution than either senile or arteriosclerotic dementia, the hormonal role is secondary. Palmer (9) states that the involutional patient reveals striking resistence to psychic trauma by developing strong protective measures, but that the difficulties which the patient faces at the time of involution represent in symbolic form the culmination of life's difficulties—failing health, diminishing vitality, impotence.

Lastly, a sense of uselessness, which is to a great degree imposed upon individuals by social customs, must never be ignored as a source of trauma.

Summary

The frequency and the importance of mental disease in later years as a social and economic problem cannot be overemphasized. It must be kept in mind that arteriosclerotic dementia, senile dementia, and, to a lesser degree, involutional melancholia are essentially mental manifestations of systemic disorders. The systemic impairment stems in part from the changes of age per se, which we have discussed, and, in part, from the accumulative injuries inevitable in a long life.

In no two instances are etiologic patterns necessarily identical. But in all instances we can find evidences of impaired cellular nutrition. Nutrition is more than vitamins, calories and the like. It involves not only intake, assimilation, transportation, and utilization of food stuffs, including water and oxygen, but also removal of metabolic debris.

Let us keep in mind that any individual is indivisible and become more concerned with the treatment of the patient and not merely of the symptoms of the disease. Far

more can be accomplished for and with the aging than for those already senile.

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Glycine-Creatine Metabolism in Its Relationship to Aging

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IN ORDER TO STUDY THE INFLUENCE OF GLYCINE INTAKE ON CREATINE OUTPUT IN DEBILITATED OLD PERSONS, DR. STERN AND MISS ASKONAS, USING 3 HEALTHY CONINVESTIGATED 2 PHYSICALLY HEALTHY BUT DEBILITATED OLD MEN, 3 PHYSICALLY HEALTHY PATIENTS UNDERGOING ELECTRIC SHOCK THERAPY, AND ONE WOMAN REPORTED AS PREMATURELY AGED WHO ALSO WAS UNDERGOING ELECTRIC SHOCK THERAPY. THEY FOUND THAT ELECTRIC SHOCK THERAPY HAD NO INFLUENCE ON CREATINE EXCRETION AND THAT THERE WAS NO INCREASE OF CREATINE EXCRETION FOLLOWING GLYCINE INTAKE EXCEPT IN THE PREMATURELY AGED WOMAN. THE LATTER SHOWED A TRANSIENT INCREASE WHICH CORRESPONDED TO THAT WHICH HAS BEEN DESCRIBED IN SYSTEMIC DISEASES OF PRIMARY MUSCULAR WASTING.

THE effect of glycine intake on creatine output undergoes characteristic changes in certain conditions associated with muscular wasting. There is a general agreement that in progressive muscular dystrophy glycine feeding is followed by increased creatinuria (Kostakov and Slauck, 11; Chanutin, Britt, and Royster, 5; Brand and Harris, 3; Cuthbertson and Maclachlan, 6; Reinhold, Clark, and Kingsley, 16; Milhorat and Wolff, 13). With regard to secondary muscular atrophies the observations are not uniform (Tripoli and Beard, 20; Kostakov, 10; Milhorat and Wolff, 14). Allinson, Henstell, and Himwich (1) studied a case of peripheral polyneuritis and showed a degree of creatinuria following glycine intake which was comparable to what had previously been seen in primary muscular disease.

Spontaneous creatinuria seems to be associated with asthenia in general since Hoagland, Gilder, and Shank (7) pointed out that spontaneous creatinuria occurs in intercurrent debilitating diseases. Moreover, cessation of gonadal function following castration is associated with spontaneous creatinuria (Schittenhelm and Bühler, 18). The same phenomenon may be seen in old men (Remen, 17; Lasch, 12).

There are also various contradictory observations on the effect of glycine intake on muscular strength in diseased and normal individuals (Brand and Harris, 3; Cuthbertson and Maclachlan, 6; Milhorat and Wolff, 13; Horvath, Kuehr, and Dill, 8; Karpovich and Pestrecov, 9).

For all these reasons it seemed important to study the influence of glycine intake on creatine output in debilitated old persons. This problem is the more interesting since it has been shown that the normal senile spinal cord shows considerable loss of anterior horn cells (Stern, 19).

MATERIAL AND METHODS

A total of nine persons was employed as subjects in this study. A woman of 56 who suffered from a depression was reported to us as "prematurely aged." This, as usual, was only a clinical impression. Her age was guessed as ten years higher by four different members of the staff. As is commonly known, there is no objective criterion of age estimation in adults. According to her, she had lost 60 pounds within one year (her present weight was 85 pounds). Malignant disease could be excluded as far as possible. Chest plate, barium series, and gynecologic examination were negative. Her blood sedimentation rate was normal. Her basal metabolic rate was normal (−1 per cent). Her routine blood chemistry showed normal results (blood

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This study, made at the Gerontologic Unit, Department of Psychiatry, McGill University, was supported by a grant from the National Research Council of Canada.

sugar 76 mg. per cent, total protein 6.32 gm. per cent, blood non-protein-nitrogen 18 mg. per cent, cholesterol 224 mg. per cent). This patient had received several electric shock treatments before this investigation was started. She also had been given 10 units of insulin before meals for three weeks before the beginning of this study.

Two men, 56 and 66 years respectively, encountered in our Old Age Counselling Center, were investigated. These two men appeared generally debilitated, but they were otherwise found healthy on clinical and laboratory investigation.

Two young healthy women of 22 and a healthy man of 40 served as controls.

Furthermore, since the patient with "premature aging" had received electric shock treatment, creatine excretion was studied in 3 patients, a man of 63 and two women, one 48 and one 38, who were under electric shock therapy but otherwise were physically healthy. One of these received 10 units of insulin before meals.

The subject was first given a nitrogen balance test for three days. Urinary excretion of creatine and creatinine was determined on three consecutive complete 24-hour specimens. After this the subject was given 15 gm. of glycine per day; after one week this daily intake was increased to 20 gm. During this time the excretion of creatine and creatinine was determined. A creatine tolerance test was carried out on 2 old subjects. Throughout the entire period of the experiment weekly dynamometer readings of the hand grip were taken. All subjects except for the 3 healthy adults were on the ordinary hospital diet. The latter were on a normal, well balanced diet. Urinary creatinine and creatine were determined on the photo-electric colorimeter according to the Birmingham-Carphin modification (2) of Folin's method. The creatine tolerance test was carried out after the patient had been on a purine-free diet for three days as described by Reiner (15).

RESULTS

The three-day nitrogen balance test showed all subjects in equilibrium. It was found that the protein intake in our average diets did not produce creatinuria. Patient McC. (fig. 1) who had been described as "prematurely aged" excreted less than 0.060 gm. of creatine on control days before and after the experiment. After glycine feeding the creatine excretion began to increase slowly until it reached a maximum of 0.320 gm. on the tenth day. After this the excretion subsided again and reached zero on the nineteenth day. Glycine intake was stopped after three weeks.

The two elderly men (figs. 2 and 3) showed no increase of creatine output following glycine feeding. None of the control cases (figs. 4, 5, and 6) who received

glycine showed any appreciable increase in the creatine excretion. The young female subjects showed considerable fluctuation in the amount excreted.

Electric shock treatment was seen to have no influence on the excretion of creatine. All three patients maintained a negligible degree of creatinuria during the course of treatment (less than 30 mg.).

In none of the investigated subjects did the dynamometer readings show any appreciable changes.

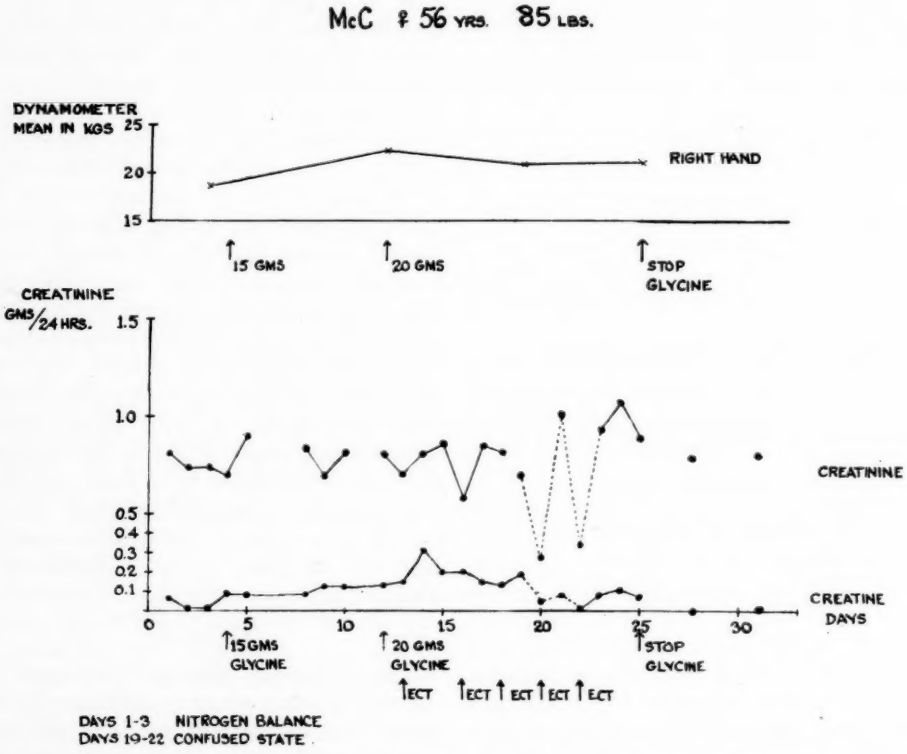

FIG. 1. Prematurely aged woman with loss of weight (see text). Note the transient increase in creatine output after glycine feeding which corresponds to that which has been described in systemic diseases of primary muscular wasting.

ECT = Electro-convulsive treatment.

The stippled lines correspond to a period when the patient was confused and urine collection was not absolutely reliable.

DISCUSSION

Except for Presenile Dementia (Alzheimer's disease), the concept of premature aging is so ill-defined that it is necessary to collect as many objective data as possible on this phenomenon. Classical neurology of the last century used the concept of abiotrophy to explain certain idiopathic diseases in which functional and developmental units of the central nervous system wasted. Von Braunmühl (21) spoke of "localized premature aging" in discussing such disorders as certain forms of cerebellar atrophy or Pick's disease.

In our present case we see that a woman who had been described by the clinician as prematurely aged showed the same metabolic peculiarity as the one seen in those rare disorders of primary muscular wasting in young people. On the other hand, there was no evidence that glycine

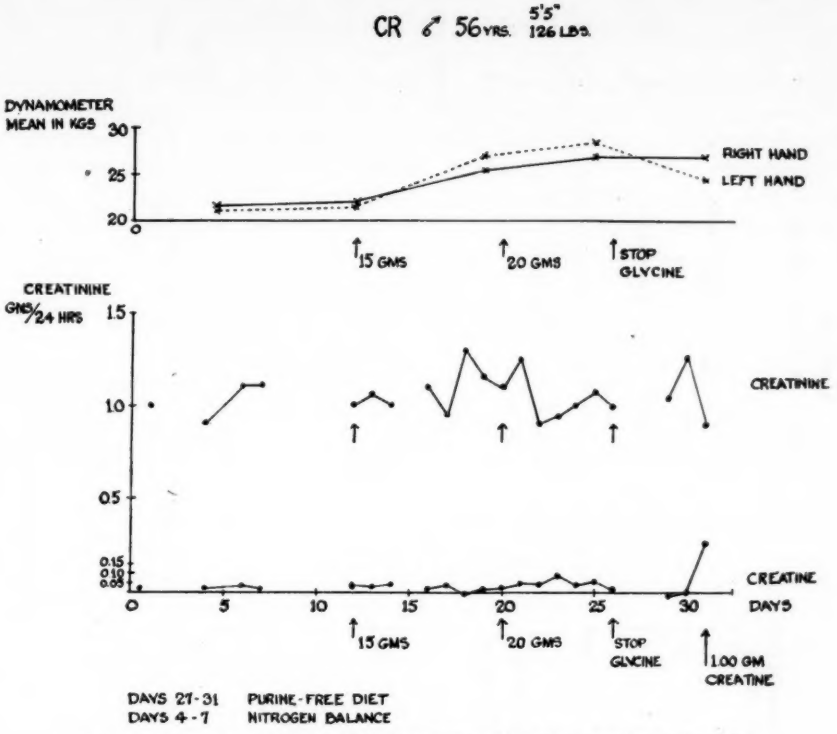

FIG. 2. Man of 56 who was debilitated but otherwise physically healthy.

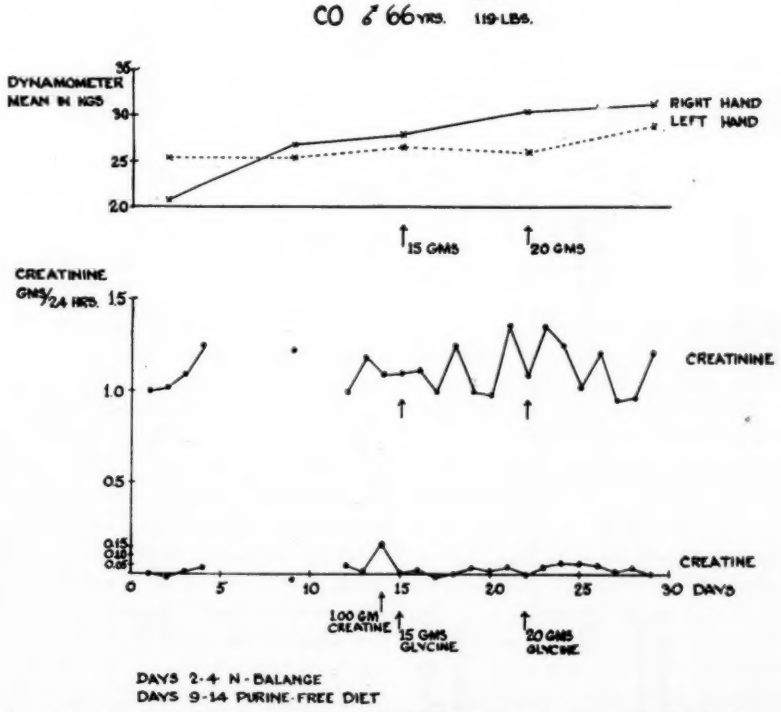

FIG. 3. Man of 66 who appeared emaciated but was otherwise physically healthy.

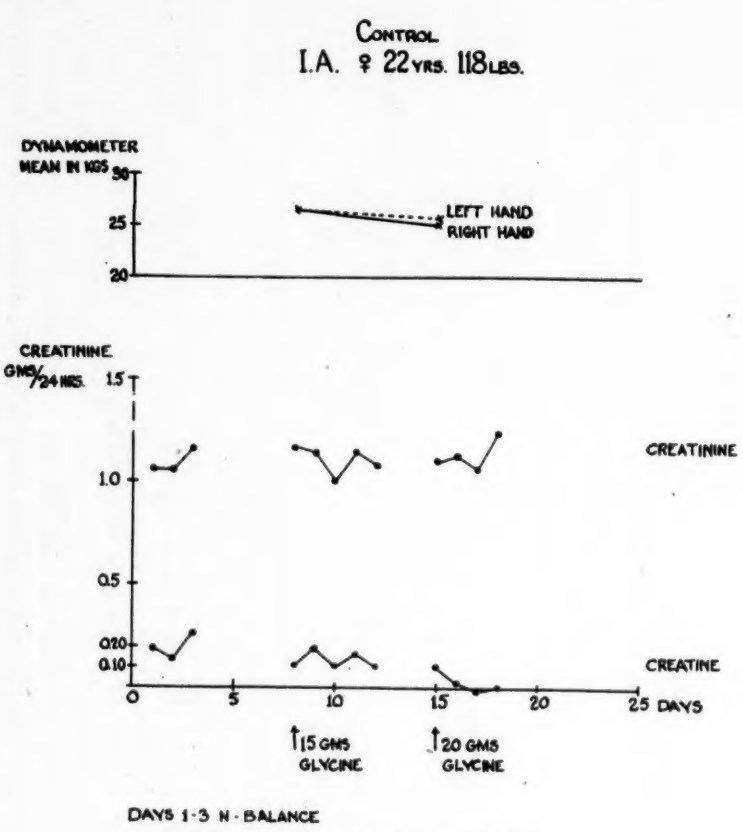

FIG. 4. Control subject—young female.

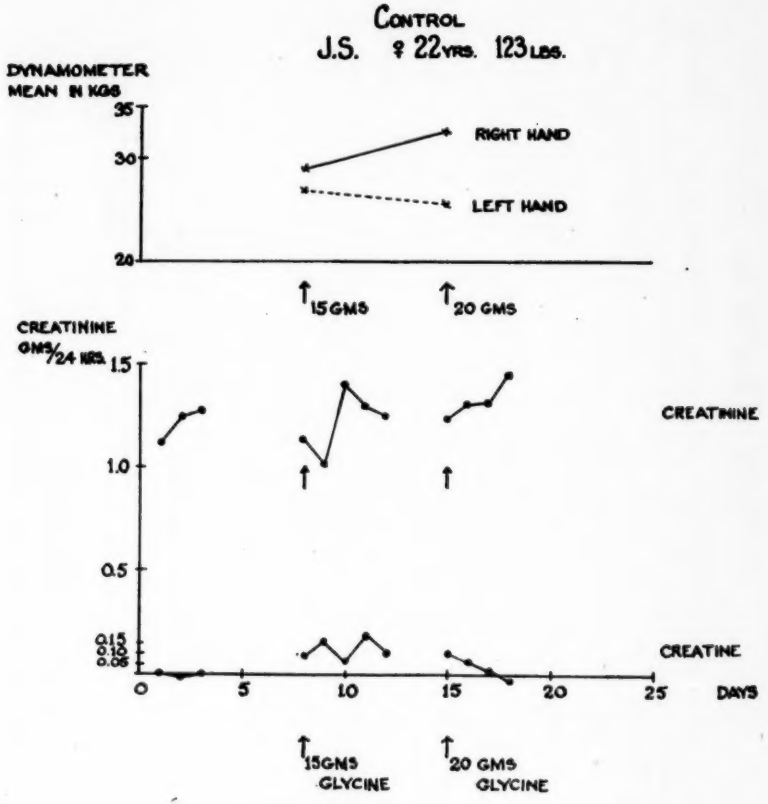

FIG. 5. Control subject—young female.

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intake increased muscular strength either in this or in any other one of the investigated subjects. The diagnosis of premature aging was as usual based on a mere impression. The patient was in hospital for an affective disorder and was intellectually unimpaired. As was pointed out, Hyperthyroidism, malignant disease, and chronic infection could be excluded. The fact that the administration of insulin was not responsible for the phenomenon is apparent since there was no creatinuria while the patient received insulin, or in one of the control cases who was on a similar regime.

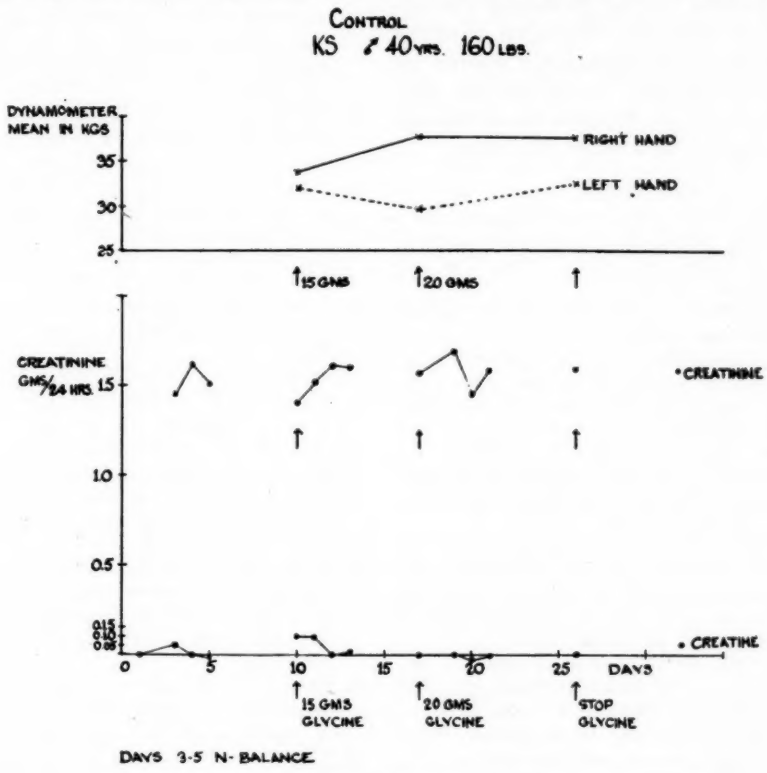

FIG. 6. Control subject—man of 40.

there is no objective criterion for age estimation in adults. The patient had undergone considerable loss of weight during the preceding year but neurologically there was no indication of any specific type of muscular wasting. There was no spontaneous creatinuria present either in this patient or in one of the two men of the higher age group. This is the more noteworthy since such spontaneous creatinuria had been reported in old age (Remen, 17; Lasch, 12), after debilitating diseases (Hoagland, Gilder, and Shank, 7) and following damage in general (Browne, Korady, and Selye, 4). The transient rise and subsequent fall of creatine excretion, also the magnitude of this increase—all these features were comparable with those observed by Cuthbertson and Maclachlan (6) and Milhorat and Wolff (13) in primary, idiopathic muscular wasting.

SUMMARY

The influence of glycine administration on creatine output was studied in 9 persons of various age groups and under various conditions. Two elderly men (56 and 66 years) who were debilitated but otherwise healthy showed the same reaction as young control subjects; there was no spontaneous

creatinuria nor any increase of creatine excretion following glycine intake. A woman of 56 who had suffered considerable weight loss and was reported as prematurely aged showed the same phenomenon as reported in diseases of primary muscular wasting; there was characteristic transient rise of creatine output following the administration of glycine. The strength of the hand grip was not appreciably altered by the intake of glycine in any of the individuals investigated. Electric shock therapy has no influence on creatine excretion.

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The Relation of Nutritional Deficiency to Impaired Libido and Potency in the Male

MORTON S. BISKIND

DR. BISKIND FOUND THAT OF 143 PATIENTS (RANGING IN AGE FROM 29 TO 61 YEARS) WITH NUTRITIONAL DEFICIENCY, DEFINITE IMPAIRMENT OF LIBIDO AND POTENCY OF WHICH THE PATIENT WAS AWARE OCCURRED IN TWO-THIRDS. OF 76 PATIENTS WHO WERE OBSERVED SUBSEQUENTLY, NUTRITIONAL THERAPY ALONE LED TO ALLEVIATION OF THE AVITAMINOTIC LESIONS IN ALL AND DEFINITE IMPROVEMENT IN LIBIDO AND POTENCY IN 62. PSYCHOGENIC FACTORS WERE INVOLVED IN AT LEAST SEVERAL OF THE FAILURES. SEVEN CASES ARE DISCUSSED IN DETAIL, TOGETHER WITH THE VARIOUS TYPES OF THERAPY USED.

AMONG the concomitants of the aging process, waning libido and potency are accepted as axiomatic. More often than not, however, this process begins long before the trophic potentialities of the gonads are exhausted, and presents a fallacious picture of accelerated aging.

Evidence is presented in this paper that this phenomenon occurs frequently as a result of a cumulative nutritional defect, which by impairing liver function secondarily induces a far-reaching endocrine disturbance. The endocrine disorder can be prevented or ameliorated by maintaining or restoring the nutritional equilibrium. Thus still another facet may be added to the already compelling body of evidence that adequate nutrition is of paramount importance in retarding onset of the degenerative diseases.

In a number of reports during the past five years various clinical aspects of the relation of nutritional impairment of hepatic function to alteration of the estrogen-androgen equilibrium have been presented (7, 9, 10, 12, 16, 17). The studies thus far published have been concerned mainly with the significance of this phenomenon in the female and its role in the etiology of menstrual disturbances related to excess estrogen (menometrorrhagia, cystic mastitis, premenstrual tension, neoplasms of the breast and uterus, postpartum subinvolution of the uterus, endocrine obesity). In other papers the role of impaired estrogen inactivation in the liver in the production of sex-endocrine disturbances in the male, with particular reference to infertility (17), testicular atrophy, gynecomastia, diminished libido, and impotence has been briefly discussed (7, 12, 18). This report is concerned with presentation of data on the latter subject in greater detail, including findings in individual cases.

In 1938, G. R. Biskind (6, 8) devised an extremely sensitive method for investigation of hepatic function in relation to the inactivation of sex-endocrine steroids. He implanted pellets of various crystalline estrogens or androgens in the spleens of castrate male or female rats. As the spleen is in the portal circulation, the absorbed material must pass through the liver before reaching the systemic circulation. Animals with pellets thus situated showed neither estrogenic nor androgenic effects from the specific steroid. However, if the spleen containing the pellet was transplanted subcutaneously and, after development of a collateral circulation the pedicle was ligated, the specific endocrine effect became evident. Both estrogens and androgens were inactivated in the livers of both male and female animals.

This method served subsequently as an efficient means of studying alterations in hepatic function. Castrated female rats with a pellet of estrogen in the spleen remained completely anestrous so long as they were maintained on a complete diet. If they were then placed on a vitamin B complex-free diet, they went into con-

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This investigation was aided by grants from the Lederle Laboratories Division of American Cyanamid Company, the U. S. Vitamin Corporation, and the Upjohn Company.

tinuous estrus, indicating that the absorbed steroid was passing through the liver. If brewers yeast were then added to the diet, the rats rapidly again became anestrous and subsequent depletion could once more produce estrus. Thus the flow of estrogen through the liver could be controlled at will by withholding the B vitamins or by restoring them to the diet (13, 14). Similar effects were obtained with animals having one ovary transplanted to the spleen and the other removed (19). Using both in vivo and in vitro technics with crystalline steroids, other investigators have confirmed and extended these original findings (21, 26, 27, 37, 38, 40, 43).

Investigation of the hepatic inactivation of androgen in dietary depletion gave a different result. Using castrate male rats with pellets of testosterone propionate in the spleen and the weight of seminal vesicles and prostate as the indicator, no significant impairment of inactivation of androgen in vitamin B complex deficiency was found (15). Thus an alteration of the estrogen-androgen equilibrium must result.

These findings in animals are in complete agreement with clinical observations by Glass, Edmondson, and Soll (24, 25) in male patients with cirrhosis of the liver, all of whom had testicular atrophy, gynecomastia, or both. In these patients, the urinary estrogen was increased and appeared in free, active form, while the urinary androgen was somewhat reduced in amount and appeared all in combined, inactive form. Wu (42) has reported histologic changes in the prostates of patients with cirrhosis of the liver resembling those produced by estrogen.

The studies showing alteration of the estrogen-androgen equilibrium in vitamin B complex deficiency led to an extensive investigation of the relation of nutritional deficiency in the human being to the occurrence of various menstrual disturbances and lesions of the breast and uterus. In three series aggregating more than 800 cases studied over a period of five years, a striking correlation was found between the lesions of nutritional deficiency and syndromes related to excess estrogen; dramatic effects on the endocrine syndromes resulted from adequate nutritional therapy (7, 9, 10, 12, 16, 18). These clinical results have been confirmed by several widely separated groups of workers (2, 28, 35, 41).

This report is concerned with a study over the same period of time of 96 cases of diminished gonadal function in the male associated with lesions of nutritional deficiency.

Case Reports

Case 1, age 61.—This patient on first examination had a severe glossitis and gingivitis, nasolabial seborrhea, keratosis of the lower eyelids, marked conjunctival injection, hepatomegaly, palmar erythema, cutaneous vascular spiders, excessive fatigability, insomnia, and numerous other symptoms related to the central nervous system. He had had little libido for a long time but paid little attention to this as he considered it a normal concomitant of age. There was definite bilateral testicular atrophy.

Intensive oral therapy providing all the water-soluble and lipo-soluble vitamins and a combination of desiccated liver and liver

extract led to rapid improvement in all the avitaminotic lesions and a very marked increase in libido and potency. The patient remarked spontaneously that he felt better than in forty years. Although the functional improvement began within a very short time of initiating treatment, there were still some residual lesions eight months later. The cutaneous and gingival lesions had healed, but tongue lesions remained and the liver, while somewhat smaller than at first examination, was still enlarged and slightly tender.

Case 2, age 54.—This patient had a severe atrophic glossitis, cheilosis, changes in the skin (a seborrheic dermatitis of the nose and malar regions, keratosis of the lower eyelids, keratosis pilaris of both upper arms, thin glistening skin in the lower extremities, palmar erythema), blepharoconjunctivitis and vascularization of the periphery of the cornea, vague but persistently recurrent precordial and gastro-intestinal discomfort, numerous symptoms referable to the nervous system (depression, irritability, insomnia, impairment of memory for recent events, easy fatigability, headaches, numbness of the right arm, lumbar backache, "restless legs"), slight but definite gynecomastia bilateral, a liver palpable at the rib margin, tender mesially, atrophy and very marked softening of both testicles. There was almost complete loss of libido and potency. For two years the diet had been severely deficient and consisted mainly of the carbohydrate foods and little protein.

Therapy including large doses of the water-soluble and lipo-soluble vitamins, desiccated liver 9 gm. per day (equivalent to 45 gm. whole liver), and addition of protein foods to the diet led to subsidence of all the symptoms and definite improvement in the avitaminotic lesions over a period of five months. At the end of this time there were virtually no subjective symptoms, the glossitis had healed with the exception of two very small areas of atrophy, the liver was no longer tender and could barely be palpated on inspiration, the gynecomastia had regressed so that it was now barely perceptible, the right testicle was normal both in size and texture, the left still soft. With the exception of two episodes which were obviously psychogenic in origin, there was complete recovery of libido and potency.

Case 3, age 43.—This man had had a bilateral symmetrical dermatitis of the hands that had resisted a variety of dermatologic therapies for two years. There were cheilosis, nasolabial seborrhea, keratosis of the lower eyelids, many large cutaneous vascular spiders, blepharoconjunctivitis, but only slight glossitis. The liver was enlarged and very tender and there was severe bilateral testicular atrophy (about one-half normal size), associated with almost complete impotence. There were numerous subjective complaints, ocular, cardio-respiratory, and gastro-intestinal, and emotional instability, insomnia, clouding of consciousness, impairment of memory for recent events, headaches, excessive fatigability, and the like. Because of the gastro-intestinal symptoms, he had been on an extremely low protein diet for several years.

Intensive nutritional therapy with all the vitamins and a protein hydrolysate led to a rapid and very dramatic change. Two months later the patient was free of all subjective complaints; libido and potency were normal. Objectively, except for some residual dermatitis on the hands, all the avitaminotic lesions had healed, the liver was barely palpable and only slightly tender, and the testicles had increased in size about 50 per cent.

Case 4.—This patient, age 42 at the first examination, was followed for three years. When first seen, his main complaint was a sore tongue which he had had for two or three years. He had a long history of allergic reactions to various foods which he had one by one eliminated from his diet, thus setting in motion a vicious cycle of nutritional deficiency and increasing allergic reactions. There were numerous neuritic symptoms, extreme fatigability,

and marked diminution in libido and potency, the latter dating back a year or more before the onset of the glossitis. He had had occasional injections of testosterone with little benefit.

On examination there were atrophy along the right margin of the tongue, gingivitis, and stomatitis with ulcers scattered throughout the oral mucous membrane and even under the tongue. There were numerous raised cutaneous vascular spiders, from 1 to 3 mm. in diameter, scattered over the trunk and arms. Both testicles were severely atrophic and softened.

Intensive oral, and later oral and parenteral vitamin B complex therapy, led to rapid subjective and objective improvement, although considerable time was consumed in increasing the vitamin dosage gradually to satisfactory levels, owing to the patient's persistent fears of allergic reactions to unfamiliar ingestants. Associated with improvement in nutritional status there was definite improvement in libido and potency which persisted as long as adequate therapy was maintained. There was gradual improvement in testicular texture. Allergic reactions were less frequent and less intense, the neuritic symptoms subsided, the glossitis and gingivitis were virtually healed, and there were only occasional mild attacks of stomatitis. The cutaneous vascular spiders gradually regressed to approximately half their original size.

Case 5, age 41.—This man, a diabetic, had had loss of libido and potency for several years. His diabetes was poorly controlled, he refused insulin and was erratic about diet, but had maintained a relatively constant (if excessive) weight. There were atrophic glossitis and gingivitis, cutaneous vascular spiders and palmar erythema, hepatomegaly, bilateral gynecomastia, and bilateral testicular softening and atrophy, more marked on the left.

Intensive oral and parenteral vitamin B complex therapy and dietary restriction were prescribed, but the former was followed erratically for several months at a time with corresponding intermissions, and the latter not at all. Despite inadequate vitamin therapy during the two intervals the patient adhered more or less to the regime, the blood sugar diminished the first time from 261 mg. to 204 mg. per 100 cc. in two months (the patient's urine was sugar-free two months later but no blood sugar determination was made at that time).

During the second session of therapy the blood sugar diminished from 283 mg. to 230 mg. in a similar period (six months elapsed between the two sessions of therapy). Both times there was prompt regression in the avitaminotic lesions and in the size of the liver and improvement in testicular texture; libido and potency were recovered within a week after therapy was started. During the eight months' interval without therapy, all the avitaminotic lesions showed exacerbation, the liver again became palpable, the blood sugar rose as indicated, and libido and potency slowly declined. All these changes were again partially reversed by therapy; the latter was not continued long enough for complete resolution of the lesions. The gynecomastia was unaffected.

Case 6.—This case was observed before the relationship of the nutritional defect

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Figs. 1 to 8 illustrate nutritional lesions of the tongue and gums associated with hepatic disturbances and testicular atrophy in cases of the type described. These photographs are all reproduced from Kodachrome; some of the more dramatic changes which occur under vitamin therapy are detectable only by variations in color and of necessity do not appear in these illustrations. However, certain of the alterations are nevertheless visible.

Figs. 1*a* to 6*a*, 2*c* and Figs. 7 and 8 represent the lesions before therapy, and Figs. 1*b* to 6*b* and 2*d* depict the changes that have occurred on therapy in association with morphologic and functional improvement in liver and gonads. Note especially partial or complete healing of the fissures and changes in the papillary surface of the tongues and the improvement in the gingival lesions in Fig. 2*d*.

Fig. 3*a* shows complete denudation of portions of the lingual surface; the raw, red areas appear dark and glistening. In Fig. 3*b* the epithelium has

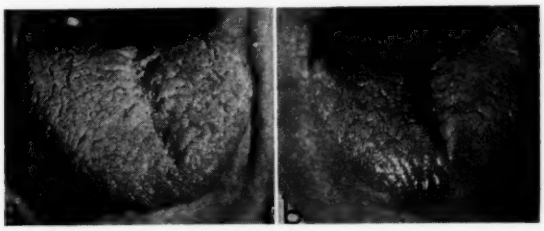

FIG. 1

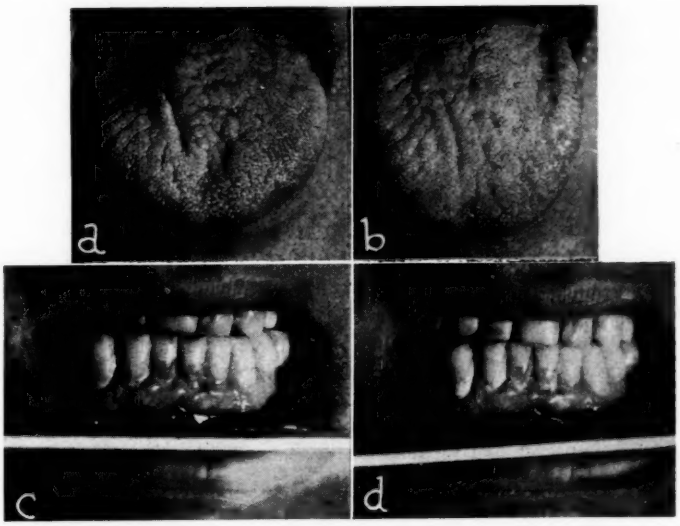

FIG. 2

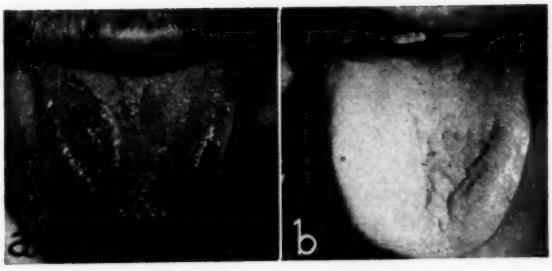

FIG. 3

regenerated completely over the major portion of the tongue and partially over the left anterior portion, which is no longer acutely inflamed. In Figs. 4*a* and 4*b* the indentation on the patient's left is at the site of an epithelioma, previously treated. Note the more uniform papillary surface after vitamin therapy in Fig. 4*b*; this change occurred along with dramatic systemic improvement. Fig. 7 illustrates the glossitis in a man who had hepatomegaly, testicular atrophy, marked diminution in libido and potency, and sterility. There is almost complete atrophy similar to that in Fig. 3*a*, along the margins. The patient whose tongue is shown in Fig. 8 had an enormous liver and severe testicular atrophy.

FIG. 4

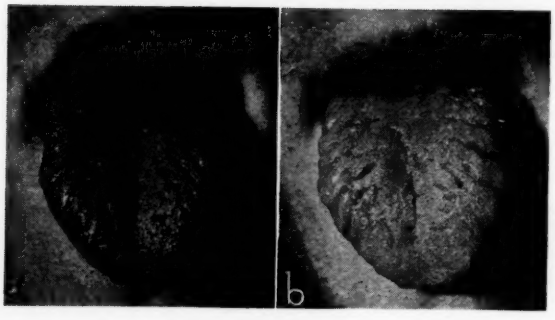

FIG. 5

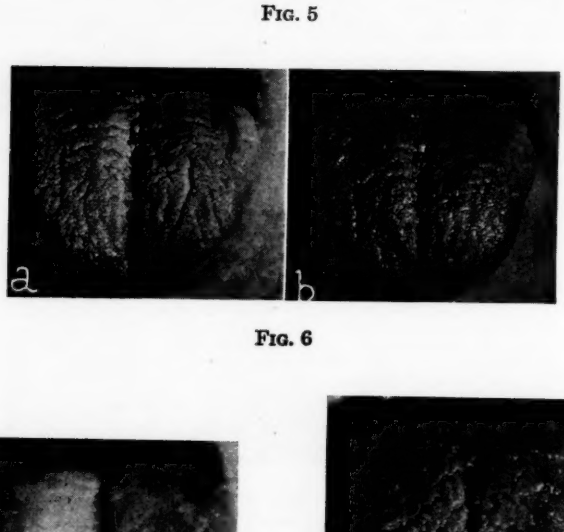

FIG. 6

FIG. 7

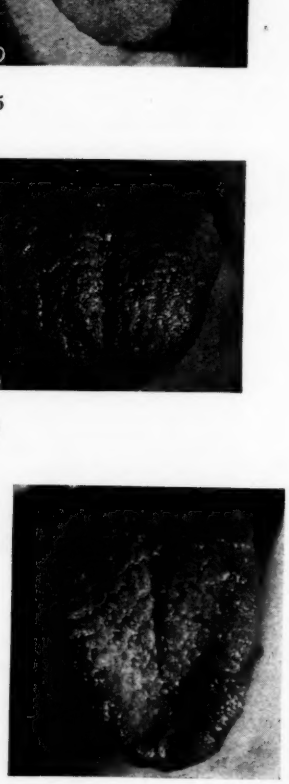

FIG. 8

to the estrogen-androgen equilibrium was appreciated and it was analyzed in retrospect. Seven years ago the patient (age 41 at the present writing), following many years of chronic enteritis, began to develop inflamed, painful, atrophic areas on the tongue. Shortly after this occurred, there was a marked diminution in libido and later complete impotence. At this time the patient noticed that his testicles had diminished to almost half their previous size and had lost their normal firm texture. Associated with the glossitis there were recurrent hypertrophic gingivitis, severe headaches, insomnia, "restless legs," injected conjunctivae, rapid visual fatigue and progressive myopia, exhausting fatigue from minor exertion, numbness of upper and lower extremities with repeated attacks of peripheral neuritis, muscle cramps, especially in the gastrocnemii, and persistent lumbar backache.

As the nutritional basis of this syndrome was only vaguely appreciated at first, the glossitis spread, the tongue became deeply fissured and painful, and the subjective symptoms worse. The patient was advised to eat liver as often as possible. Each time this was included in the diet, the tongue healed, partly or completely, within one to two days, only for the lesions to recur within another day or two. So tenuous was the equilibrium in this patient that even a moderate excess of physical exertion would lead to denudation of areas of the tongue within a few hours.

This patient was placed on an oral vitamin B complex preparation derived from liver, following which moderate improvement in the symptoms occurred, and later parenteral B complex was added every second day. Striking subsidence of all the symptoms related to the nervous system then occurred, associated with equally impressive improvement in the glossitis. Soon thereafter there was a marked improvement in libido and potency and a gradual restoration of the normal firm testicular texture (but only a slight increase in size occurred, no doubt owing to shrinkage of the tunica vaginalis).

Subsequently it was found necessary to maintain the patient continuously on whole liver and vitamin B complex by mouth and daily or bidaily injections of the crystalline vitamin B factors. Undoubtedly because permanent damage to the gastro-intestinal tract resulted in this case from the chronic enteritis and the associated nutritional defect, persistent impairment of intestinal absorption occurred, which explains the necessity for the indefinite maintenance of parenteral therapy.

During the seven years that this patient has been under observation there was an invariable correlation between libido and potency and the nutritional state. There were many exacerbations and remissions of the signs and symptoms of deficiency during that time owing to persistence of the enteritis, and the endocrine symptoms regressed or improved concomitantly (with only a slight time lag). During one of the exacerbations, a unilateral mastitis developed. This subsided with improvement in the nutritional lesions. Over this long period the nutritional equilibrium gradually lost its earlier tenuous character, and libido and potency have been correspondingly more nearly stable.

Case 7, age 38.—This man had been in a German concentration camp for three years. His main complaint was complete impotence. He had severe glossitis and gingivitis, as well as other signs of avitaminosis, hepatomegaly, marked atrophy and softening of both testicles. On nutritional therapy similar to that already described, there was moderate subsidence of the avitaminotic lesions and recovery of potency in two months; the liver was now smaller although still palpable, and the testicles were somewhat more firm although still smaller than normal.

Of 143 patients with nutritional deficiency in this series, ranging in age from 29 to 61, definite impairment of libido and potency of which the patient was aware, occurred in 96. The actual incidence of this disorder in B avitaminosis is probably higher than indicated, because not a few

patients become aware of previous impairment only when improvement results from therapy, and this series includes 20 patients who were seen only once. Definite testicular atrophy occurred in 67. Glossitis, hepatomegaly, and testicular atrophy appeared simultaneously in 58. Of 76 patients who were followed subsequently, nutritional therapy alone led to subsidence of the avitaminotic lesions and definite improvement in libido and potency in 62.

In at least several of the 15 failures, psychogenic factors were undoubtedly operative; this must of course always be taken into consideration in the treatment of disorders of this type. Eleven cases were known to be complicated by sterility. However, the actual occurrence of sterility in cases of this type cannot be assessed from the figures here given, since sperm counts were made only in those cases in which the patient came for consultation for that reason. The nutritional therapy of infertility per se has previously been reported (17).

Discussion

Testicular atrophy is a diagnosis rarely made by clinicians, despite the fact that this defect has long been associated with nutritional impairment and with cirrhosis of the liver (20, 24, 36, 39). Even in diabetics, in whom diminished libido and potency have been known for decades to be frequent concomitants of the metabolic disturbance (22) testicular atrophy is rarely noted, despite its high incidence.

While it has been shown in animals that there is no necessary correlation between functional impairment and morphologic alteration of the liver (and this is also apparently true clinically) a surprising number of the patients in the series reported here had enlarged livers, easily accessible to palpation. Yet in only a few had the hepatomegaly previously been diagnosed. The frequent association of lesions of nutritional deficiency, especially glossitis, with hepatomegaly and testicular atrophy, suggests that the presence of any one of these lesions should lead to investigation for the others.

As already indicated, in the diagnosis and treatment of impaired libido and potency, the possible occurrence of psychogenic factors must always be kept in mind. In cases in which such factors are dominant, amelioration of the nutritional defect will of course have little effect on the sexual function and even the administration of testosterone is of little or no help. It is necessary to treat both nutritional and psychogenic disturbances simultaneously, as physiologic recovery of testicular function will be of no avail in the presence of an inhibiting psychic disorder, while alleviation of the mental conflict alone will not permit normal tissue function in the presence of a physiologic defect. The more fundamental implications of psychogenic disorders in relation to nutritional deficiency will be discussed elsewhere.

In a number of instances in this series, both husband and wife had syndromes related to excess estrogen as a result of nutritional deficiency. In the wife the excess estrogen usually greatly increased libido (in an occasional case almost to the degree of nymphomania), while simultaneously libido and potency in the husband were reduced. This of course inevitably led to considerable marital conflict. Simultaneous nutritional therapy in husband and wife diminished libido to normal levels in the wife and increased libido and potency in the husband, with a corresponding mutual improvement in morale.

As indicated elsewhere (12), the effect of nutritional deficiency on testicular morphology and function represents a composite of two effects: a direct effect on the cellular metabolism of the gonads owing to deprivation of nutrients essential to cell respiration, and secondary alteration of the endocrine equilibrium, which indirectly affects the testis. Undoubtedly in a given case the two effects are intermingled and inseparable. Thus, deprivation of various vitamins causes disturbances of testicular morphology (34), and administration of estrogen has similar effects (1, 23).

Among somatic alterations reported in a previous study on the female, redistribu-

tion of body weight was not infrequently striking on intensive vitamin B complex therapy (16). Loss of fat deposits on hips, thighs, and abdomen and diminution in size of breasts occurred without loss of body weight, so that clothing of smaller sizes could be worn comfortably. This effect also occasionally occurs in the male and was seen in four cases of this series in which the body contours resembled those of the Froehlich syndrome. The normal male contour was restored over a period of many months, in one case despite an actual gain in weight.

Gynecomastia occurred in 10 cases of this series. In 4 of these there was a superimposed cystic mastitis. The mastitis and associated tenderness cleared up promptly with adequate therapy, but some gynecomastia often persisted. It appears that once the epithelial tissue has become sufficiently hyperplastic, withdrawal of the original stimulus only occasionally leads to complete regression. In addition to its well known occurrence in cirrhosis of the liver, already mentioned, gynecomastia was also noted in our troops in the Pacific who were captured by the enemy and maintained for long periods on extremely deficient diets (30, 32, 33).

Bean (3, 4, 5) has reported that the cutaneous vascular spiders and palmar erythema formerly associated mainly with liver disease and with pregnancy also occur in nutritional deficiency, and he has shown that estrogen is an inciting factor. Administration of estrogen to patients with these lesions caused exacerbation of those already present and the appearance of new ones. Withdrawal of estrogen led to regression of the cutaneous phenomena. He further showed that histologically the vessels of the latter resemble the spiral arteries of the endometrium. Virtually every patient in the group reported here had the spiders or the palmar erythema or both.

In a previous report (12) it was indicated that usually only slight or moderate improvement in these lesions occurs on nutritional therapy and complete regression has not been seen. However, there is no question that the development of new lesions is impeded or prevented. And occasionally there is a very striking diminution in the size and vascularity of the spiders on vitamin therapy, as in one patient (age 59) who had a raised spider 5 to 6 mm. in diameter on his nose. For years bleeding had occurred even from the slightest friction, such as on contact with a pillow while sleeping. Not only was there a striking diminution in size and prominence of the lesion after two months of intensive nutritional therapy, but bleeding no longer occurred even from vigorous irritation. Often too, there is partial regression of palmar erythema associated with healing of the avitaminotic lesions.

Many patients with nutritional deficiency and associated hepatic dysfunction have disturbances in cholesterol metabolism with elevation of blood cholesterol and decrease in percentage of cholesterol esters. Usually these patients, especially the diabetics and hypertensives among them, are warned not to eat liver, eggs, or other cholesterol-rich foods. The chief result of this interdiction is further to impair the nutritional status.

When these patients are placed on a regime combining the available crystalline vitamins and desiccated and cooked whole liver, there is usually a dramatic reduction in blood cholesterol, despite the greatly increased intake (18). Thus, a high blood cholesterol represents impaired hepatic metabolism and is not merely a reflection of increased intake. This factor is also applicable to changes in blood cholesterol in many cases of thyroid disturbance and explains the poor correlation frequently seen between basal metabolic rate and the blood steroid levels. Here too the hypercholesterolemia reflects primarily the associated impairment of nutritional status.

Therapy

As discussed at greater leng elsewhere, there are three requisites for adequate nutritional therapy: complete therapy, intensive dosage by routes assuring adequate utilization, and persistent administration.

Many failures result from disregard of one or more of these principles.

Because of the use of single drugs has a strong tradition in modern medicine (in reaction to the unscientific "shotgun" therapy that persisted until two or three generations ago), it is common practice to administer thiamine, riboflavin, niacinamide, or pyridoxine alone in large doses in an effort to counteract an apparently predominant deficiency of one of these factors.

But single deficiencies are impossible in clinical medicine. Not only are clinical deficiencies always multiple, but it should be pointed out that a pure deficiency of a single vitamin has never been produced even in animals. At the present state of our knowledge, production of an uncomplicated deficiency of a single factor is impossible. For instance, to produce thiamine deficiency, an animal would be placed on a vitamin-free diet to which has been added all the available pure vitamins except thiamine. Thus, the deficiency produced is a deficiency of thiamine plus that of all the other factors not yet isolated. And when thiamine is administered to such an animal and an effect noted, this cannot be assessed as an uncomplicated function of thiamine; it merely indicates what thiamine can do in the absence of other essential factors. When all the essential nutrients have been isolated, it will be necessary to reassess the functions of each.

In the human diet, factors which lead to loss of thiamine, for instance, inevitably lead to loss of other substances that occur with it and have similar solubilities, or are also labile to heat, alkalinity, or oxidation. Similarly, conditioning factors (31) which operate to produce nutritional deficiency even on an optimum diet, tend inevitably to produce deficiencies of several factors at once.

Not only are deficiencies multiple, but the administration of single nutritional factors (or even of a combination of a few of them) not only is usually ineffective but may actually lead to serious disturbance of a tenuous nutritional equilibrium and precipitation of new avitaminotic lesions. Those familiar with the history of the early use of niacin in the treatment of pellagra will recall the glowing preliminary reports of rapid healing of the skin lesions and the glossitis, soon to be followed by pessimistic accounts of the appearance of secondary lesions, such as cheilosis and peripheral neuritis. The addition of an adequate natural source of nutritional factors to the therapeutic regime led to prompt subsidence of the lesions. Similarly, in a recent study on treatment of the peripheral neuritis of beri-beri in prisoners of war, administration of thiamine alone failed to affect the neuritis, although there was definite amelioration of this lesion in patients who received the whole B complex (29).

Depending on the original nutritional status and response of the patient, adequate nutritional therapy might require 2 or 3 capsules a day of a therapeutic formula type of preparation, providing intensive dosage of the crystalline water-soluble factors and A, D, and E. In addition, a vitamin B complex preparation consisting of a fortified or unfortified natural source or sources, preferably liver, is essential. This must be given in a dosage sufficient to provide material derived from at least 45 gm. and occasionally as much as 150 gm. of the fresh natural source a day.

For this purpose two types of vitamin B complex preparations are especially valuable: (1) nutritional extracts of liver fortified with crystalline B vitamins—these preparations contain the total aqueous, or 80 per cent alcohol-insoluble fraction of liver, or a combination of the two (lipoid factors of liver, which also comprise essential nutritional elements may be included [11]) and are given in dosages representing from 80 to 120 gm. of fresh liver a day (usually 9 to 12 capsules or equivalent amount of liquid); and (2) desiccated whole liver, either fortified with B vitamins or unfortified—usually at least 9 gm. (eighteen 0.5 gm. capsules or tablets) is given daily, sometimes more. The minimal dose provides the equivalent of 45 gm. fresh whole liver a day.

Desiccated liver, being unfractionated, provides probably the best available source of the as yet unidentified factors essential to nutrition (11), although some slight losses probably occur from drying and oxidation. It must be given in relatively large doses to be effective; these dosages are, however, quite feasible. All the products are given in divided doses after meals.

A number of severely deficient patients require parenteral therapy in addition, with a frequency varying from daily to three times a week. This usually provides, in each injection, thiamine 10 to 60 mg., riboflavin 5 to 10 mg., pyridoxine 5 to 20 mg., calcium pantothenate 5 to 50 mg., and niacinamide 50 to 250 mg. Sodium ascorbate may be mixed with the B vitamins in the same syringe. Parenteral liver extracts, which are purified mainly with a view to increasing the antianemic potency, are not satisfactory for nutritional therapy; even the so-called crude preparations contain only insignificant amounts of the B factors in a volume feasible to inject (12).

Even after all avitaminotic lesions have healed and the secondary disturbances are under control, it is necessary to maintain the patients indefinitely thereafter on at least 5 to 10 times the maintenance amounts for persons who have never been deficient, often much more.

Summary

Impaired hepatic function on a nutritional basis leads to alteration of the estrogen-androgen equilibrium, owing to failure of the liver to inactivate estrogen in deficiency of the B vitamins, while it continues to inactivate androgen. Evidence is presented that lesions of avitaminosis B are associated clinically with impaired libido and potency in the male and that these functions may be restored with complete, intensive, and persistent nutritional therapy.

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The Effect of Age on the Carbohydrate Metabolism of Tissue Homogenates

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DR. REINER HAS STUDIED SOME OF THE ENZYMATIC CHANGES INVOLVED IN THE PROCESS OF AGING IN BRAIN AND LIVER TISSUE, USING RATS AS EXPERIMENTAL ANIMALS. THESE STUDIES ARE CONCERNED WITH THE OVERALL CARBOHYDRATE METABOLISM, INVESTIGATED BY MEANS OF REINFORCED HOMOGENATES. HE FINDS THAT THE OXIDATION OF CARBOHYDRATE BY BRAIN IS VIRTUALLY CONSTANT THROUGH THE SECOND YEAR OF LIFE, AFTER WHICH IT DECLINES SHARPLY. ANAEROBIC UTILIZATION, ON THE OTHER HAND, HAS A PRONOUNCED MAXIMUM IN ANIMALS FROM 2 TO 4 MONTHS OLD, AND THEN SLOWLY AND STEADILY DECREASES. THIS ENYZME PATHWAY THEREFORE SEFMS ROUGHLY TO PARALLEL THE PROCESSES OF MATURATION AND SENESCENCE. THE CHANGES IN THE METABOLISM OF LIVER TISSUE ARE PRONOUNCED IN GOING FROM EMBRYONIC TO POST-NATAL LIFE. THEREAFTER THEY ARE MUCH SMALLER AND OF DOUBTFUL SIGNIFICANCE. AS A CONSEQUENCE OF THE ABOVE FINDINGS, CLOSER INVESTIGATIONS OF SPECIFIC ENZYMES, ESPECIALLY THOSE CONCERNED WITH ENERGY ACCUMULATION AND TRANSFER, ARE INDICATED. THE NEED TO STUDY DIRECTLY THE MECHANISM OF SELF-RENEWAL OF ENZYMES IS DISCUSSED.

THE tissues of adult organisms may be considered as examples of the steady state in open systems (14, 15). Systems in such a state should be able to maintain themselves indefinitely, provided certain factors of the environment—particularly the supply of nutriment and the removal of waste products—are kept constant. It is clearly inaccurate to speak of living tissue as wearing out if they are so constituted.

The failure of cells to maintain and renew themselves, which we observe in the phenomenon of aging, points to a disturbance of the mechanism for protoplasmic self-renewal. No obvious and specific environmental factors which could account for this failure have as yet been detected. All those environmental fluctuations which we observe are too small to tax the homeostatic mechanisms of the organism and its component cells. It seems most logical at this time to investigate the internal mechanisms which are involved in this process.

Failure of crucial enzymes in a cell to be reproduced or to reproduce themselves would account for the observed effects. The enzymes have hitherto been studied in an indirect manner by determining at various times the chemical composition of the tissues which results from their varying activities (3, 8, 10, 17). It is easier to obtain such experimental material, however, than to interpret it fruitfully. It seems necessary to study the activities of the cellular enzymes directly as a function of age.

The enzymes concerned with protein synthesis are probably the most critical for the aging process. Unfortunately, relatively little is known about them (1), and they are not easy to investigate directly. The simplest to study are the enzymes concerned with carbohydrate metabolism, in view of the enormous amount of knowledge available concerning them (2, 6, 9, 11, 16, 18). They are potentially important for the problem because they constitute the mechanism for furnishing the energy which the cell needs to perform any of its functions.

This report deals with a preliminary investigation of carbohydrate metabolism in brain and liver tissue of the white rat. To furnish some background for subsequent research, the overall utilization of glucose by oxidation and glycolysis was

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Investigation for this paper was done at the Department of Physiology, University of Minnesota Medical School.

selected for study. The rat was chosen as an omnivorous animal whose general physiologic and metabolic pattern resembles that of man.

Previous studies (13, 19, 20) have shown how tissue homogenates may be used in such a way as to reflect approximately the maximum potential enzyme activity. This technique of course ignores the complications which are due to the molecular architecture of the cell. It has been employed, despite this limitation, because it is readily controlled and standardized. On the other hand, enzyme studies of the truly intact cells of multicellular organisms are at present almost impossible unless one is willing to be exceedingly liberal in defining the term intact.

Materials and Methods

The rats used were chiefly of the Sprague Dawley strain. Some La Jolla rats and a few crosses between the two strains were included but showed no significant differences from the Sprague-Dawley animals. Most of the rats were born and raised in our own colony. They were fed a standard diet of Purina Fox Chow, supplemented with carrots and lettuce. Only animals which were apparently completely free of disease were used for experiments.

To obtain maximal activity, the tissue homogenates were reinforced with a number of co-factors, such as adenosine triphosphate, diphosphopyridine nucleotide, and cytochrome C. The method of preparation of homogenates and co-factors and the composition of the final experimental suspension are given in detail in previous publications (13, 19, 20). As usual, oxygen consumption was measured in Warburg vessels with alkali in the center well, while glycolysis was measured in similar vessels in terms of the CO_2 driven off from bicarbonate buffer by the acid produced, the gaseous atmosphere being a mixture of 5 per cent CO_2 and 95 per cent nitrogen; 0.028 M glucose was used in all cases as the substrate.

In order to determine the dry weight of the tissue, an aliquot of 2 ml. of each homogenate was pipetted into a tared evaporating dish, dried for an hour in a 100 C. oven, and placed into a vacuum desiccator to cool and dry to constant weight. The usual method of expressing rates of enzyme activity involves the Q_{O_2} and the $Q_{CO_2}^{N_2}$, defined respectively as microlitres of oxygen consumed per hour per milligram of dry weight of tissue used and as microlitres of carbon dioxide evolved per hour per milligram of dry weight of tissue used. The dry weights were therefore determined on all experimental material in order to avoid error because of possible variations in the water content of the tissues with age.

Experimental Results

The age range of the animals studied runs from embryos near term to animals over 2 and in some cases over 3 years. In presenting the data this range has been divided into intervals of six months, except for the youngest animals, which are grouped into 1 month and 2 month inter-

TABLE 1. RESPIRATION AND GLYCOLYSIS OF BRAIN AND LIVER TISSUE OF THE WHITE RAT AS A FUNCTION OF AGE

Age, Months	Embryos	0–1		2–4		4–6		6–12		12–18		18–24		Greater than 24	
		♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Brain Q_{O_2}		14 ±0.8	—	15 ±1.3	15 ±2.6	15 ±2.5	16 ±1.0	16 ±2.0	15 ±0.5	15 ±1.7	18 ±1.0	15 ±2.3	16 ±2.5	10 ±1.6	—
	10	14 ±0.8		15 ±2.2		16 ±1.8		15 ±1.5		16 ±1.6		15 ±2.5		10 ±1.6	
N_2 Q_{CO_2}		55 ±6.5	—	76 ±4.5	79 ±5.6	67 ±3.5	70 ±2.0	61 ±2.5	63 ±0.8	59 ±7.4	61 ±6.0	54 ±2.9	52 ±4.0	60 ±5.1	—
	27	55 ±6.5		78 ±5.4		69 ±2.8		62 ±1.5		59 ±6.9		54 ±3.2		60 ±5.1	
Liver Q_{O_2}		7 ±1.0	—	10 ±1.3	11 ±1.7	12 ±3.0	11 ±0.0	11 ±1.6	12 ±1.0	11 ±1.5	12 ±1.5	10 ±1.1	11 ±1.0	9 ±2.2	—
	7	7 ±1.0		11 ±1.8		12 ±2.0		12 ±1.8		11 ±1.5		10 ±1.1		9 ±2.2	
$Q_{CO_2}^{N_2}$		29 ±3.3	—	19 ±2.3	19 ±1.6	18 ±1.0	18 ±1.0	20 ±2.0	18 ±1.7	18 ±1.5	19 ±2.5	18 ±2.7	19 ±2.3	19 ±2.6	—
	29	29 ±3.3		19 ±2.0		18 ±1.0		19 ±2.1		18 ±1.9		18 ±2.7		19 ±2.6	
Dry Weight of Tissue Used															
Brain	2.3	3.2	—	3.9	3.6	4.0	3.7	4.2	4.0	4.2	4.1	4.3	4.1	4.4	—
Liver	4.2	5.4	—	5.9	5.9	5.8	5.9	5.7	6.0	5.7	5.9	5.9	5.9	5.5	—
Number of Animals		6	—	3	3	2	2	5	6	11	6	15	4	10	—
	10	6		6		4		11		17		19		10	

The values are microlitres of gas exchange per hour per milligram dry weight of tissue. For glycolysis, CO_2 evolved is equimolar with acid (mostly lactic) produced; 22.4 microlitres of CO_2 represent 1 micromole of lactic acid. Dry weights are in milligrams, and refer to the amount of tissue used in one experimental sample. All values are means for the age and sex group; all individual determinations were performed in duplicate.

vals, and the oldest, which constitute a single group labelled "Greater than 24 months." Most of the animals in the last group were older than 2.5 years. The use of a single category for animals older than 2 years is justified by the very close cluster of the activities of animals in this set around the mean value.

The animals are further divided into male and female, except for the embryos; in the latter case a litter of embryos of both sexes was pooled to obtain enough tissue for the experiment.

The data obtained from the 83 animals studied are presented in table 1. The figures are mean values for the groups indicated by the headings at the top of each column. The figure joined to each mean value by a

± sign is the average deviation in the set of individual values from which the mean was calculated. The average deviation is defined as the sum of the absolute values of the figures in a set divided by the number of such figures; like the standard deviation, it is a measure of the degree of scatter of the values around the mean.

Under each pair of male and female entries is another figure which is the mean value for all animals of both sexes taken together in that particular age group. The mean dry weight of the brain and liver tissue used in one experimental vessel is given for each age group. The number of animals in each group is enumerated, separate entries being employed for males and females and followed by the total of both.

Each of the individual experimental figures whose means are given in the table was itself the average of duplicate values.

Discussion

The most striking effect of old age per se is shown by the values of oxygen consumption for brain tissue. Here the embryonic level has risen to the adult value during the first month of post-natal existence. This value is maintained until the age of the animals exceeds 2 years. It then drops to a considerably lower level. Unfortunately, no females greater than 2 years of age and otherwise uniform with the rest of the animals were available for study. A group of males and females probably in this age range was obtained after they had been used in a lengthy dietary experiment in another laboratory. Birth dates were not available, so that the ages could only be approximated. Both males and females clustered around values significantly higher than those found for our known "Greater than 24 months" group. Accordingly, in view of the uncertainties connected with the age, strain, and previous regimen of the animals these data were discarded.

The glycolysis of the brain homogenates shows a marked variation with age, but of entirely different form. In a sharp rise from birth, a peak value is attained between 2 and 4 months, followed by a slower decline. After two years, there is a slight rise, which on the basis of the standard deviations is of doubtful significance. It is worth noting, however, that the distribution of values in both groups ("18-24 months" and "Greater than 24 months") was quite skewed, so that the degree of overlap between them is much smaller than is indicated by the use of the mean deviations.

For the liver tissue, age variation is far less noteworthy, except for the drop of glycolysis in the first month from a rather high embryonic value. The oxygen consumption seems to show some regular variation, with a maximum somewhere between 4 and 12 months; but the differences are too small to be given much weight.

It will be noted that the dry weight of liver is uniformly greater than that of brain. This is probably due to the high proportion of connective tissue, which does not contribute to metabolic activity. It may be that the presence of this inert material is masking significant age changes, especially if it varies with age.

The experiments just reported show that the overall metabolism of certain tissues changes with age; and this would encourage the investigation of specific enzymatic reactions in greater detail. In particular, reactions involving the formation or transfer of high-energy phosphate bonds would seem to be worth study. Detailed studies of specific enzymes as a function of age have been reported recently (12). Unfortunately, they only extend through one month.

Since brain tissue in vivo is highly aerobic in its metabolism and suffers severely from oxygen lack, the oxygen uptake figures for brain are probably the most significant. On this basis, it might be inferred that the changes in the carbohydrate metabolism of brain are not the primary aging changes since they do not appear until the animals are fairly old.

On the other hand, the variation in brain

glycolysis with age is of some interest. During a period when the ability to utilize glucose aerobically is constant, the ability to utilize it anerobically attains considerable heights and then declines. The time relations are quite different from those found for resistance of the animal to anoxia, however (4, 5, 7), since the latter appears to decline steadily and rapidly from birth. It seems reasonable today that we have here a significant symptom of aging, though probably not a primary part of the mechanism of aging.

It is clear the from results that enzymatic changes at least accompany the aging process. These changes cannot be attributed to alterations in permeability of the cell surface or other structural factors, since the work was done with distilled water homogenates. They cannot be attributed to deficiencies in low-molecular weight compounds, since all soluble co-factors were added in excess. Unless some unknown inhibitors are involved, the changes must therefore be in the enzyme proteins themselves—either in amount, state, or both. These findings point to the desirability of studying the mechanism of self-renewal of the enzyme proteins. Such studies are now under way.

Summary

The aerobic and anaerobic glucose metabolism of rat brain and liver tissues have been studied, as a function of age, by the method of reinforced tissue homogenates.

The respiration of brain is essentially constant from birth for about two years, after which it shows a sharp decline.

The anaerobic glycolysis of brain rises to a pronounced maximum between 2 and 4 months, after which a slow decline occurs.

Age changes in the carbohydrate metabolism of liver, with the technique used, are not sufficiently great to be judged with certainty as significant.

The significance of these results is briefly discussed. The necessity for turning attention to the mechanism of self-renewal of proteins is indicated.

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FOUNDED IN 1682, THE ROYAL HOSPITAL PROVIDES SHELTER FOR APPROXIMATELY FIVE HUNDRED PENSIONED REGULAR SOLDIERS OF ENGLAND. DR. HOWELL DESCRIBES THE HISTORY, THE BUILDINGS, THE ADMINISTRATION, THE LIFE THE PENSIONERS LEAD, THE ADMISSION REQUIREMENTS, AND THE METHODS OF NURSING CARE, AS WELL AS WARTIME EVENTS AND THE BROADER GERONTOLOGIC ASPECTS OF PROBLEMS AT THE ROYAL HOSPITAL, CHELSEA.

IN THE middle of London, down by the river Thames, is a quiet oasis where stately buildings of warm red brick stand among pleasant gardens and lawns of green grass. Here some five hundred aged veterans of the British Army live together in their declining years. Dressed in their summer uniform of scarlet frock coats and great three cornered hats, the army uniform of 1700, the old men make a vivid splash of colour as they pass through the streets of London or sit in the spacious grounds of the Royal Hospital.

This is their last home, where old soldiers can amuse themselves, cultivate their plot of garden and fight all their battles over again in comfort as they wish. For those without relatives and for those whose relatives do not want them, the Hospital is a real sanctuary and haven of rest. A return to the military atmosphere gives them a sensation of security and order which many of them have found lacking in civilian life.

HISTORY

The standing professional Parliamentary Army of England was first formed in 1660. Before this time, all soldiers had been volunteers who served either during some period of war, or under the King's personal attendants during peace. When regular engagement became the rule, it was felt that those men who had spent the best years of their life in the military service of their country deserved some support in their old age. In addition to this, it was found that many discharged soldiers, accustomed to weapons and violence, turned robber, footpad, or highwayman for lack of other employment. Some, not used to earning an honest living, became beggars and exhibited their wounds to gain the pity and the money of passers-by. Tradition says that the kind heart of Nell Gwynne, the mistress of Charles II, was touched by this neglect of the men who had fought the battles of their country. It may have been her influence which persuaded the king to found the Royal Hospital in 1682 to provide for the veterans of his army.

The money which paid for the land on which the Hospital stands and for the cost of the building was obtained by the Paymaster-General, Sir Stephen Fox, chiefly by deductions from the pay of officers and men in the army. About £7000 was given by the king and a certain amount was raised by private subscription, but this was little compared with the sum provided by soldiers. The Royal Hospital is, therefore, in no sense a charity.

By the time that the building was completed, it was found that the number of men eligible for admission was greater than expected. Five hundred pensioners were then taken into the Hospital and the rest were granted a regular sum of money to maintain them until a vacancy should occur. From this arose the system of out-pensions which is still in existence. Of course, today the out-pensioners number many thousands, since every man who has served his full term in the regular army is eligible for a pension on his discharge.

The building was designed by Sir Christopher Wren, the famous architect,

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many of whose churches were destroyed by German bombs during the recent war. Under him, as Clerk of Works, was Robert Adam, who also left his mark on London. By the time the Hospital was finished in 1692, Charles II was dead, his brother and successor James II in exile, and the new king, William III, patron. Hence the Latin inscription over the colonnade in the Centre Court mentions all three monarchs.

In Subsidum et Levamen, Emeritorum Senio, Belloque Fractorum, Condidit Carolus Secundus, Auxit Jacobus Secundus, Perfecere Gulielmus et Maria Rex et Regina,— MDCXCII.

Buildings and Administration

The Hospital surrounds three great courtyards, the centre one of which is open to the south, giving a pleasant vista down to the river. The east and west wings off this centre court contain the "long wards" in which the pensioners live. The lateral courts contain the houses in which the staff of the hospital live and certain offices, as well as quarters for the old men. On the outer side of the eastern courtyard lie the offices of the pensions department of the War office. On the outer side of the western courtyard are the Quartermaster's stores, with the site of the infirmary and the nurses' home behind them. To the south lie the grass lawns of the south grounds, stretching down to the embankment of the river. To the southeast are the parklike Ranelagh Gardens, a former famous pleasure ground of the Regency period. Both of these are included in the Hospital curtilage, and make pleasant walks for both pensioners and residents.

The chapel and the great hall make up the north side of the central courtyard. These have fine proportions, measuring 198 feet in length by 37 feet in width. The chapel is panelled with old oak and has a handsome carved and pillared altar screen with fine altar gates of lime wood by the King's carver. The centre of the reredos is a panel of polished wood from Jerusalem, representing the Star of Bethlehem. On the domed ceiling above the altar is a fresco of the Ressurrection.

The benches in the chapel are placed longitudinally, with special pews for the various officers living in the Hospital. Above the rear entrance is the lofty musicians gallery around the carved organ case. Many captured standards and trophies normally hang in the chapel, but these were removed for safe keeping during the war. The communion plate dates from the time of James II and is extremely handsome in shape and workmanship.

The great hall was used as the dining hall of the Hospital until 1814, but is now the recreation room of the pensioners. It, also, is wainscotted in oak up to the level of the high windows and likewise has a musicians' gallery. At one end is the dais on which the officer's dining table formerly stood. Here, above the panelling, is a large fresco of Charles II on horseback, trampling down various mythical figures representing treason and anarchy. Around the walls hang many pictures and portraits of royalty and distinguished soldiers who have been associated with the Hospital. The original heavy dining tables are now used for games, supplemented by a few billiard and bagatelle tables, which are

very popular with the old men.

Outside the chapel and the great hall is a colonnade, of tall white stone pillars. It covers a pleasant walk, with a narrow bench on which pensioners may sit in the shade. On cold or windy days the old men prefer to stay in the long wards. These contain the bunks placed back to back, with a corridor between each row. Tall windows look out onto the square. There are two great fireplaces in each row, always burning, for the Chelsea pensioner is a chilly mortal. Each bunk or cubicle contains a bed, a table, and shelves; it has a chair and a wooden chest or trunk in which uniforms can be kept. The door and window space is so arranged that there is an aperture which may be shut, curtained off, or open. In this way, each man can attain the exact amount of privacy which he may desire at any time.

The fine oak staircases which lead to the upper wards in the first and second stories are plain but dignified, with a small tread and easy rake to the steps, so that veterans can mount them without difficulty.

Pensioners have their kit issued from the Quartermaster's store, which privides uniform, underwear, and boots. Incidentally, it is amazing to see how many garments an old man can wear in cold weather. No less than seven layers, which had to be removed before a veteran's chest could be examined, have been counted. Among other amenities, there is a regular issue of beer and tobacco which is very welcome, especially in these days of shortage. Pensioners receive pay varying from a basic 1/9d to 10/6d a week, according to rank, employment, and duties performed. For those who have grown too feeble to continue longer as noncommissioned officers of the Hospital, retired pay is awarded. There is usually work available for pensioners who desire occupation as officer's servants, messengers, hospital police, orderlies in the Quartermaster's store or Adjutant's Office, and so on. Money earned in this way adds to the pay and is consequently very welcome.

The Hospital is administered by the War Office under the direction of "My Lords and others, Commissioners of the Royal Hospital," one of whom is the Director General of Army Medical Services. It is commanded by the Governor, a Field Marshal or full General, whose appointment is the reward of a distinguished military career. He is assisted by a Lieutenant-Governor, who is a Major-General. Under them are six pensioner officers, known as Captains of Invalids, each of whom commands a company of pensioners.

Also attached to the Hospital are several serving military officers, including the Chaplain, the Adjutant, the Quartermaster, and two medical officers. The senior of these is known as the Physician and Surgeon, the junior as Deputy Surgeon. These titles date back a number of years and have an interesting history. Under the officers are the warrant officers—the Sergeant-Major, the Quartermaster-Sergeant, the Sergeant Cook, and the Hospital Sergeant. All these are former army warrant officers with long and honourable military careers. They are among the most hard working people in the Hospital.

Medical History

The medical side of the history of the Royal Hospital is not without interest. Many of the early pensioners were admitted while suffering from wounds or the effects of disease acquired campaigning in various parts of the world. The description "worn out by military service" was applied to many entrants in those days.

Since there was no regular medical corps in the army, civilian physicians and surgeons were engaged to attend to the wants of the pensioners. These posts became highly coveted. For example, William Chesleden, the leading surgeon of his day, held a position at the hospital from 1737 to 1752. The famous John Hunter is known to have walked the wards at Chelsea and dressed the old men's wounds. A century later, Dr. Daniel Maclachlan became the Physician to the hospital. He published a

celebrated book on "Diseases and Infirmities of Advanced Life" as the fruit of his experience. This geriatric classic is still well worth reading today. In fact, it is more helpful than many modern textbooks on old age.

Turning to modern times, we find that the medical officers have been supplied by the army. After the first world war, Majors Thompson and Todd pioneered in new work on the care of the aged. They published two valuable papers in Lancet during 1922, one on blood pressure in old age, the other dealing with the diseases of Chelsea Pensioners. Ten years later, Major (now Brigadier) Lipscombe compiled his book "Diseases of Old Age," which summarised all that was then known on the subject. It is still a valuable source of references on the work of the past. About the same time, Dr. Macdonald Critchley was granted facilities for his research on the central nervous system in the aged, which was the basis of his celebrated Goulstonian Lectures at the Royal College of Physicians. This work remains today as the only really serious contribution to neurology so far made in gerontology.

Arrangements for nursing pensioners when they are ill have a comparatively recent origin. They were conceived, designed, and organized by no less a person than Florence Nightingale, the founder of modern nursing, who visited the hospital soon after the Crimean War (1854 to 1856). Her first step was the introduction of Long Ward Nurses, soldiers' widows or daughters, who could mother the old men when they were well and care for them when sick.

Later an infirmary was set up in an adjacent house, formerly the residence of Sir Robert Walpole, (Prime Minister 1721 to 1742). Nearby were built houses for the senior medical officer and for the Matron of the infirmary, who, incidentally, was entitled to be married. A nurses' home did not arise until many years had elapsed. For several decades, the pensioners were nursed in vast four poster beds by women who had not been fully trained in nursing. At length, properly trained nursing sisters were introduced to take charge of the wards. In more recent years, Long Ward Sisters became responsible for the supervision of the healthy pensioners and any out-patient treatment needed. The original infirmary of some eighty beds had a nursing complement of a matron, four sisters, and eighteen nurses. There were also five or six male orderlies under a trained ward-master. The patients are under the care of the Deputy Surgeon, who, as the senior medical officer, is chiefly concerned with administration.

Since the pensions department of the War Office has its headquarters at the Royal Hospital, it is the duty of the Physician and Surgeon to advise on the medical aspects of claims for disability pensions a responsibility which takes up much of his time. The medical officers are also responsible for the medical care of the resident staff and their families—a function which can be very responsible at times. Nevertheless, both posts are greatly coveted and usually fall to the lot of picked officers in normal peacetime.

Pensioners

The pensioners of the Royal Hospital normally number 558 in all. But damage to buildings sustained during the war stopped all admission of new recruits for a time, so that there are less than usual at present. Recruiting has recently started again to build up the strength to its pre-war figure. Each applicant must be a former regular soldier of good character, disabled by wounds or age from earning his living.

In most cases, the Commissioners insist that the man should be in reasonably good health and capable of looking after himself. Those ailing in body or mind are usually not accepted unless their record and circumstances happen to be very unusual. It is considered unwise to take men who will need admission to the infirmary at an early date. In consequence, the pensioners are a fit, healthy body of picked old men, reasonably active in body and mind.

For this reason, they were found to be perfect material for research on various normal physiologic findings in old age. In 1944, when my last survey of all the healthy pensioners took place, the youngest was 56 and the oldest 91; in the infirmary was a pensioner of 94. At the beginning of the war there was a man who marked his one-hundredth birthday in the hospital by making a very good speech at a small celebration given in his honour. He was still capable of getting out of bed and walking a few steps; his mind was reasonably normal within its limits. Unfortunately, he was killed by enemy action just before his one hundred and first birthday—probably Hitler's oldest victim.

Pensioners are not restricted in their movements, and may get leave to go and stay with friends or relatives if they wish. One man used to spend a few days at the Ritz whenever he got tired of the life at Chelsea. He had qualified for no less than four different pensions during a long life, having left the army early and gone into various civilian employments. Another pensioner would supplement his pay by taking small parts in various films where his expert knowledge of horses could be utilised. Provided that a man attends such functions as the weekly church parade, his pay parade, and medical inspections, he can come and go as he pleases. Only a small number, however, wander far afield. The most frequent excursion is the nightly trail to local public houses for a glass or two of beer.

Wartime Events

The happenings of the recent war caused many changes at the Royal Hospital. During the "blitz" on London, some twenty-six bombs exclusive of incendiaries fell either on the buildings or in the grounds. A barrage balloon winch stationed in the south grounds received a direct hit. In consequence one of the crew became for a time the youngest inmate of the hospital infirmary and the only member of the R.A.F. to enter it. On another occasion four delayed action bombs fell close to the infirmary, one of them splitting the wall in one place. The patients were evacuated without incident to the other part of the building until the bombs had been removed. The east wing of the long wards was struck on one occasion, fortunately without causing casualties, because most of the men were in air raid shelters at the time.

Later, in 1941, a land-mine registered a direct hit on the infirmary, leaving a deep crater where the four-story building had stood. Eighteen people were killed, among them several members of the nursing staff. As a result, the infirmary had to be reconstituted in the mansion of Mr. Anthony Rothschild near Leighton Buzzard, forty miles out of London. Finally, during the "flying-bomb" attacks, the hospital was struck by a rocket, which demolished many buildings and killed a number of people, including the Physician and Surgeon, Major Napier. By a strange coincidence, the rocket landed in the same spot as that struck by one of the last bombs to hit London in the 1914 to 1918 war. The amount of damage was very different, however.

At present, the infirmary occupies a site at Leatherhead, twenty miles south of London, where the sick pensioners are looked after by a local doctor who was a medical officer at Chelsea for a period during the war. Most of the new recruits are admitted to this building until Chelsea is repaired and rebuilt ready to accommodate them. The present wards in London can only accommodate about one hundred fifty men, so it is fortunate that there is room elsewhere.

Gerontology

My memories of the period of five years as Deputy Surgeon at Chelsea are mainly happy ones. The hospital is a little world of its own, set apart in the middle of busy London. Wartime conditions knit officers, staff, and pensioners together more closely than ever before. The chief complaint of

the men was that the blackout interfered a little with their customary nightly excursion for a glass of beer. They took little notice of the bombs. Medically speaking, it was a place where much would be learned from experienced sisters and nurses. With ample control material, there was opportunity for careful clinical investigation of patients and time for meditation over the problems they raised. The fact that no pathologic facilities existed merely acted as a stimulus.

The first problem to arise was the management of the patients suffering from bronchitis, by far the most frequent disease. This often went on to broncho-pneumonia, the onset of which was hard to determine. Even when sulphonamides improved the lung condition, the pensioners frequently developed congestive cardiac failure. Treatment of this complication with digitalis and mercurial diuretics was often only partly successful, since some of the cases then manifested cerebral symptoms, associated with falling blood pressure.

All this had been described by my predecessor, Daniel Maclachlan, nearly a hundred years before. It raised enough questions to provide occupation during the whole of the subsequent five years, and some of the research which it stimulated is still unfinished. Such points as the normal physical signs associated with healthy old age, normal variations of the blood pressure in advancing years, the significance of palpable arterial thickening, the customary levels of temperature in old men, and the significance of a raised sedimentation rate all had to be considered and determined.

The absence of any knowledge of the normal physiologic variations of old age caused each step forward to entail two steps backward, or so it seemed. Fortunately, Chelsea pensioners are ideal research material and also provide many clinical problems for consideration. No wonder that my predecessors, from Hunter and Chesleden onwards, enjoyed the duties at Chelsea. Nowadays, when interest in the care of old people has at last been aroused, it seems that two hundred and fifty years' experience is not without value. Many of the modern ideas have been standard practice at Chelsea for years.

Summary

For two hundred and fifty years the Royal Hospital, Chelsea, has given shelter to the pensioned soldiers of England. Admittance requirements are that a soldier be of good character, incapable of earning his living, and in reasonably good health.

The large Hospital, with a capacity of five hundred men, is administered by the War Office. It is commanded by the Governor, assisted by a Lieutenant-Governor, under whom are six Captains of Invalids, each of whom commands a company of pensioners. A Chaplain, Adjutant, Quartermaster, Physician and Surgeon, and Deputy Surgeon are also attached to the Hospital.

Chelsea pensioners have provided a background for valuable research material in gerontology for many years.

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The General Physiology of Aging—A Review

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DR. LANSING HAS ATTEMPTED IN THIS REVIEW TO CORRELATE THE MAJOR PART OF THE EXISTING LITERATURE ON THE GENERAL PHYSIOLOGY OF AGING. STUDIES ON THE PERMEABILITY CHANGES WITH AGE, THE FEW EXISTING VISCOSITY STUDIES, AND OTHER PHYSICAL MEASUREMENTS ARE BRIEFLY EVALUATED. CONSIDERABLE EMPHASIS IS PLACED ON THE INORGANIC CHEMICAL CHANGES WITH AGE; A THOROUGH DISCUSSION OF THIS ASPECT OF AGE CHANGES IS POSSIBLE BECAUSE OF THE VOLUME OF EXPERIMENTS THAT HAVE BEEN DONE. SOME ORGANIC CHEMICAL CHANGES ARE CONSIDERED AS WELL AS THE SIGNIFICANCE OF AGE PIGMENTS, METABOLIC CHANGES, AND GROWTH. EXPERIMENTAL STUDIES BEARING ON THE ROLE OF GROWTH REGULATION IN AGING ARE ALSO EXAMINED.

THE subject for this review, after careful consideration, was selected for several reasons. First, the writer is primarily concerned with the general physiology of aging. Second, the literature on this phase of the aging problem is badly dispersed and should be brought together. The last and chief reason is based on the similarity between the underlying philosophies of general physiology as a specialized branch of physiology and a broad view of the problem of aging.

General physiology works on the assumption that living material, regardless of species and stripped of secondary differentiations, is essentially the same. Similarly, aging, because it is essentially universal in occurrence and because its pattern is quite uniform in different species, in all probability involves a common underlying mechanism.

This view is set forth quite succinctly by Heilbrunn (31), who stated, "In the last analysis, according to any theory, senescence is due to protoplasmic changes, changes which occur in individual cells."

If we accept this view that the process of aging in different species involves essentially the same protoplasmic changes, it becomes difficult to entertain the classical view of Osler that "man is as old as his arteries" or that of Bogomolets (14) in stressing the significance of connective tissue in aging. Undoubtedly these tissues do age and the consequences of their aging to the organized individual are most serious. Nevertheless it must be remembered that many organisms that possess neither arteries nor connective tissue systems age and die.

Aging is a problem of cellular change—of unfavorable change in the ability of protoplasm to maintain itself by self-synthesis. This review is an attempt to bring together at least the major portion of the existing data on this subject. Heilbrunn's (31) chapter on age and death in his textbook of general physiology constitutes an excellent source of reference material.

PHYSICAL MEASUREMENTS

Reliable data on the physical cellular changes with age are seriously lacking; only a handful of observations have been made, and the majority of these are neither technically sound nor adequately supported. Permeability studies are not consistent. Benedict (7) on the basis of indirect observations concluded that permeability decreases with age in Vitis Vulpina and other plants. He stated that "the duration of life is directly linked with the degree of permeability in that part of the living cell which places it in contact with the universe about it, and that as the activities of life proceed, the cell is gradually entombed by an inevitable decrease in the permeability of its protoplasm."

Ensign (26), using the same venation method, was unable to confirm Benedict's

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results and sharply criticized the technique. Later, however, Telefsen (91) and Finardi (28) conducted experiments which apparently confirmed Benedict's data. MacDougal (56) described a lowered permeability of the cell membranes of century-old cells of the plant Carnegia gigantea.

That permeability changes with age are not simple is shown by the work of Weber (99, 100, 101) on Spirogyra and Ranunculus. Weber concluded that old full-grown cells of Spirogyra are more resistant to alcohol solutions than young cells, but that young cells are more resistant to urea solutions than old cells, i.e., the permeability of Spirogyra cells to alcohol decreases with age while the permeability to urea solutions increases with age.

It was observed in Ranunculus that permeability to urea solutions in very old cells reverts to the low level of young cells. Similarly, Marklund (58) studying Elodea found that young cells are relatively impermeable, that old cells are more permeable, but that very old cells revert to the relative impermeability of the young cells. This phenomenon of reversion of very old cells to the embryonic condition, as Heilbrunn (31) observed, characterizes many phenomena.

Nordenson (71) studying aging of the human lens concluded that permeability of the anterior surface of the lens decreases to some extent with age. Kopaczewski (44), without any experimental data, stressed the importance of a decrease of permeability with age in a concept of aging based upon the behavior of colloids. In this respect, Kopaczewski is an ardent supporter of Rusicka and Marinesco, who have emphasized the similarity between aging of colloids and protoplasmic aging.

Studies of the viscosity changes of protoplasm with age are virtually non-existent despite their potential value in interpreting protoplasmic behavior. Weber (101) concluded that young cells are relatively fluid, that viscosity increases to middle life, and that the fluidity of young cells is re-established in very old cells. Belehradek (6), using his temperature coefficient method, decided that viscosity of protoplasm increases with age. While this view is reasonable, no conclusion can be reached until more precise data are available. MacDougal (56) was unable to find any change in hydrogen ion concentration in cell sap of extremely old plant cells. Apparently no data exist on specific gravity measurements with respect to age, physical properties of cell membranes, nuclear membranes, or nuclear contents.

Organic Chemical Measurements

A limited amount of information is available on the aging of enzyme systems. Sekla (85) has found the activity of esterolytic enzymes increases from birth to middle age but gradually declines with advancing age to a level comparable to that which exists at birth. The enzyme activity of wild stock Drosophila is high when compared to a short-lived vestigial mutant. Falk, Noyes, and Sugiura (27) analyzed the lipase activity of extracts of whole rats at different ages and found that lypolytic activity of tissues increases from embryonic to adult life and then decreases with advancing age to the original embryonic level.

According to Vermehren (94) the phos-

phatase activity of plasma decreases with age, while Lightbody (53) determined that the arginase activity in the livers of white rats decreases with age. A decrease in acid soluble phosphates was found by Kay (41). Similarly, Pincussen, Reed, and Visscher (77) ascertained that the acid soluble phosphates in muscle, kidney, and liver increase in early life but decline with age. Kaplan and Greenberg (40) also decided that acid soluble phosphates increase up to maturity then fall with advancing age. Inorganic phosphates as well as ATP fall with age.

Cahane (17) found that the cholesterol content of the lens increases with age while the water content decreases. Bernstein (10) in a general survey of the problem pointed out that cholesterol and insoluble globulins increase with age in the lens while the water content decreases with age. As might be expected, the ascorbic acid content of the adrenals and liver decreases with age (Mulinos, Pomerantz, and Lojkin, 69).

Benetato, Oprean, and Munteanu (9) discussed the inability of old tissues to synthesize hexosephosphoric esters and adenylpyrophosphoric acid. Analysis of soluble protein nitrogen in rat muscle, kidney, and brain revealed that this protein nitrogen is low in muscle and kidney of newborn rats, increases to a peak in adult animals, and falls back to the newborn level in senility. Soluble protein nitrogen in rat brain showed no change from birth to adult life but a sharp drop in old age. Tissue protein changes with age were studied by Schenck and Wollschitt (83) and amino acid analyses were made by Block (13).

In a survey of the age variations in protein composition of cardiac muscle and brain tissue in the rat, Medvedeva (64) found that insoluble and soluble proteins gradually increase with age with the insoluble fraction showing greater change. Hydrophilic tissue colloids dècrease with age to the extent of 43 per cent in cardiac muscle and 15 per cent in brain tissue. Robertson and Dawbarn (79) made a detailed study of the nucleic acid changes with age in the small intestine, liver, skin, kidney, and other organs of the sheep. The conclusion was reached that the nucleocytoplasmic ratio falls with age.

Of particular interest in the problem of protein metabolism in aging are the observations of Lehotsky (52) and Nikitin (70). Lehotsky concluded that there was an increase in the alkali dissociation constant or constants of tissue proteins in aging and related such changes with a colloidal concept of aging. Nikitin believed that there is a decreased rate of protein synthesis in old age. That such a change should exist is entirely reasonable on an a priori basis.

The colloidal concepts of aging should be considered briefly in this section. Some of the leading proponents of the view that protoplasmic aging follows the same pattern as colloids are Rusicka (81), Marinesco (59), and Mühlmann (67). A similar approach to the problem of aging was adopted by Ehrenberg (25) and Benetato, Oprean, and Munteanu (9). Lansing (51) criticized the colloid theory of aging on the basis that protoplasm, unlike colloids that are static systems, is in a perpetual state of flux and that its constituents are constantly being renewed. The point was made that aging is a product of breakdown of the capacity for self-synthesis.

Herzfeld and Klinger (32), in a lengthy discussion of the biochemistry of aging, developed an interesting but unsupported concept of aging. They proposed that the density of proteins at the cell surface increases with age with a resultant decrease in permeability of the cell membrane. Such interference with free exchanges across the cell surface were held to be highly significant in the production of aging. The view was also offered that the density of proteins at the cell surface constituted a mechanism for self-regulation of cell volume-cell surface ratios.

Inorganic Chemical Measurements

Probably because of the relative ease with which studies of inorganic changes

can be effected, there is a considerable volume of material available. Calcium has been studied quite extensively over a period of years. As quantitative analytical methods for calcium have been refined relatively recently, much of the work done more than a few decades ago is of doubtful value. Unless proper precautions are taken, magnesium is a serious contaminant in calcium precipitations and some of the data obtained in early work probably were conditioned by this factor.

Novi (73) reported that the calcium content of the brain of the guinea pig at birth is low but that toward the end of the life span calcium increases markedly. In the dog, however, Novi found that the calcium content of the brain is high in the fetus, very low in the young animal, and very high in the old dog. These data parallel the results obtained by Lansing (unpublished), who worked with the rat brain. When appropriate corrections are made to adjust for myelinization, the apparent drop from fetal to early life is obviated.

Cahane (16) concluded that the amount of calcium per gram of fresh muscle of the guinea pig, dog, cat, and rabbit decreases with age. It is apparent from Cahane's data that the majority of animals referred to as "old" were actually immature or young adult animals.

Burger and Schlomka (15) described calcium increases with age and Sorsby, Wilcox, and Ham (89) found increases of calcium with age in the sclera of the cat. Calcium decreased during development according to these investigators. Delbet and Bretau (24) determined that while calcium increases with age, magnesium tends to decrease proportionately.

Changes in blood calcium with age have been investigated by Greisheimer, Johnson, and Ryan (29), Parhon and Werner (75), Cheymol and Quinquand (21), Watchorn (98), and Kirk, Lewis, and Thompson (43). Marked calcification of arteries with age were described by Hesse (33). Simms and Stolman (86) in an extensive investigation on changes with age in human tissue electrolytes described a consistent pattern of calcium increase with age.

Bazilewitch and Prawdina (5) observed that there is a shift with age of calcium from bone to the soft tissues. Vermooten (95), studying the origin and development of calcium plaques in the renal papilla, concluded that this form of calcification is a function of senescence. Barnes (4) observed that calcification of the heart and kidney of the rat is a function of age as well as other factors. Blatherwick and Medlar (12) noted that rats fed 5 per cent irradiated yeast developed calcified kidneys, aortae, and renal calculi. The life span of these rats was short. On the other hand, Campbell, Bessey, and Sherman (18) found that rats fed a low calcium diet appeared normal, the second generation animals were small, unable to rear their young, and appeared senile at one year of age.

Schecter (82), in a program of study on the role of calcium in the aging of unfertilized Arbacia eggs, concluded that experimental reduction of the calcium content of the medium results in significant prolongation of the life of these eggs. It is difficult, however, to justify Schecter's view that the unfertilized egg is a living organism with a definite life span of its own, and that the disintegration of the unfertilized egg is an index of its senescence.

Molisch (66) in his excellent book on longevity of plants repeatedly cited the trend to calcium deposition with age in various plants and suggested that there might be a relation between this phenomenon and a possible decrease in permeability. This view is supported by the experiments of Arens (3) in which the localization of calcium in cells of Elodea was determined by immersion of leaves in sodium oleate. Characteristic crystals of calcium oleate formed at the cell membranes and the concentration of the crystals there increased with age.

In a similar study, Lansing (47) traced the calcium changes with age in Elodea. It was found that calcium increases with

age in the cell cortex. Microincineration studies by Lansing (48) on a rotifer, a planarian, and a toad showed that calcium increases with age in the cell cortex of these animals. The suggestion was made that this peripheral calcium increase with age might produce a permeability decrease with resultant interference with metabolism. Using the short-lived rotifer as experimental material, Lansing (49) showed that reduction of the calcium content of the medium appreciably increases the life span of the rotifer. Similarly, experimental removal of calcium from the cells of the rotifer by means of sodium citrate results in more than a 50 per cent increase in life span.

Changes with age in cation content of tissues other than calcium have not been very extensively analyzed. Bertrand and Beauzemont (11) traced the changes with age in zinc content of the body. They found that the zinc content of the newborn animal is at a high level, that it falls very abruptly during the suckling period, increases moderately until adult life, and finally reaches a peak level in the senile animal comparable to that of the newborn.

According to Benetato and Ciurdariu (8) potassium in the rat brain drops about 20 per cent from adult to senile life while potassium in the gastrocnemius muscle of the rat falls about 10 per cent. Underhill and Peterman (93), tracing the relation between age and amount of aluminum in tissues of dogs, found that the fetal liver, kidney, brain, and lung contain very little aluminum. Young puppies contain demonstrable amounts of aluminum, which increases to a maximum in old dogs.

Delbet and Bretau (24) reported a trend toward decreased amounts of magnesium in senility but their analytical methods appear to be of doubtful value. Smythe and Miller (87), studying the iron content of the albino rat throughout the life cycle, found that the percentage of iron per gram of body weight after forty days of life remained constant. On the other hand, Zondek and Carp (104) reported significant increases in iron content with age.

Age Pigments

If, as has been frequently proposed, aging is due to progressive intracellular accumulation of substances which either obstruct metabolism or are toxic to the cell, it would seem reasonable to expect to find microscopic evidence of such accumulation. Such observations have been made during the last fifty years, but the evidence is far from conclusive. Hodge's classical observations (34) made over half a century ago on bee and human nerve cells have been repeatedly cited. He found that there is a pronounced increase with age in the amount of pigment granules present. Later Mühlmann (68) stressed the significance of pigmentation of nerve cells with age. More recently, MacDougal (56), in emphasizing the significance of lowered permeability of cell membranes in century-old plant cells, described increased intracellular granulation and silica crystal formation.

Zeglio (103) concluded that yellow pigments increase with age in the nerve cells of man. That the so-called age pigments may not develop as a function of age was brought out by Kuntz (46), who observed that presence of melanotic cytoplasmic pigmentation of ganglion cells is a common phenomenon after thirty years of age in man. These pigments often occur as a cap over the nucleus but as their concentration increases they tend to fill the cytoplasm. Disease seemed to be a more important factor than age in determining the presence of pigments in ganglion cells.

Truex (92) in studies on morphologic alterations in human Gasserian ganglion cells concluded that the occurrence of pigmentation as a function of age is variable but that calcification is most common after forty years. MacNider (57) using Herxheimer's Sharlack R stain for lipoids found that stainable lipoids appear in the cells of the proximal convoluted tubule of old dogs but are not present in young dogs. Extensive deposition of pigments in the

ganglion cells of Agriolimax and Limax was described by Szabó and Szabó (90).

Considerable doubt as to the validity of describing pigmentation of cells as a function of age was the theme of an article by Altschul (2). He described the yellow and brown pigments as separate entities and believed that the yellow pigments are a product of incomplete metabolism. Apparently these pigments may occur early in life during disease.

Tissue Respiration

While in general it appears that tissue respiration decreases with age, there is some evidence indicating that respiration may either be unaltered in aging or may even increase. Numerous studies have shown that oxygen consumption of animals decreases with age. Typical of these and relatively recent is the work of Davis (23) which demonstrates that the oxygen consumption of rats declines steadily with age.

The extensive and classical investigations of Child on senescence, rejuvenescence, and metabolic gradients in lower invertebrates were evaluated in a comprehensive report by Watanabe and Child (97). Their studies with the polyclad worm, Stylochus ijimai, indicated that the respiratory rate decreases with age and that experimental sectioning increases the respiratory rate. Respiratory rate is in effect Child's index of age status in the majority of his studies. It would seem that the validity of his conclusions depends upon the justification for using rate of respiration as an index of senescence or rejuvenescence. Hyman (36) in support of a long series of investigations described a decrease in oxygen consumption as a function of age in Planaria. Similarly, Obreshkove (74) studying the Cladoceran, Simocephalus, found that oxygen consumption falls with age and reached the rather obvious conclusion that aging involves a decreased rate of dynamic processes.

Plants too reveal a decrease in respiratory activity with age. Lilienstern (54) found that the reduction capacity with methylene blue and methionine in Elodea cells is decreased with age. Hover and Gustafson (35) working with corn, sorghum, wheat, and oats showed that the rate of respiration of these plants decreases with age but tends to increase in extreme age.

Pearce (76) has shown that liver, kidney, and cardiac muscle have a lower oxygen consumption with advancing age and that liver undergoes the most marked change, cardiac muscle next, and kidney shows the least change with age. Victor and Potter (96) found a decrease in oxygen consumption in lymphoid tissue of old mice. They observed that old mice have a higher aerobic and anaerobic glycolytic rate than young mice.

Carroll (20) in tissue respiration studies with the chicken found that shortly after hatching of the chick the respiratory rate of the liver increases, remains constant for about a month, and then falls progressively through the first year of life, after which the respiratory rate remains relatively constant. According to Adams (1) skin of the albino rat not only reveals a decrease in oxygen consumption with age but also water, phospholipid, and total lipid decline with age to a constant level.

Growth

That the problem of growth bears directly on the problem of aging has been recognized since the beginning of modern scientific interest in gerontology. As early as 1908 Minot (65) stressed this relation in his book entitled *The Problem of Age, Growth, and Death*, and more recently Cowdry (22) has evaluated the difference in aging potentials of intermitotic and postmitotic cells.

Bearing on the relation between growth and aging are the experiments of a number of workers who have found that the life span of invertebrates is increased by starvation or semi-starvation. As early as 1903 Kellog and Bell (42) investigated the effects of limitation of food supply on the size, fertility, activity, and mortality of a

silk worm, Bombyx mori. An apparent increase in longevity through starvation was described.

Northrup (72) studied the effect of prolongation of the period of growth on the total duration of life of Drosophila melanogaster. Sterile eggs raised from the time of hatching on an adequate yeast-glucose-agar diet had an average length of life considerably longer than flies maintained on a limited diet until the tenth day of life. Northrup observed that the increased longevity was due to prolongation of the period of growth and that the length of the adult period was unaltered.

Kopec (45) concluded, on the basis of experiments on caterpillars of Lymantria dispar L., tadpoles, and Drosophila, that prolongation of the total duration of life is effected, not by an increase in the period of adult life but by an extension of the period of growth. Actually, in the Drosophila experiments, the period of adult life was decreased by intermittent starvation.

Ingle (37) induced semi-starvation in Cladocerans by the simple expedient of diluting the infusion medium with pond water. Very marked increases in longevity were observed in the semi-starved animals and Ingle attributed this effect to delayed maturation. A similar observation was made by Ingle, Wood, and Banta (38) in a more extensive series of experiments, and it was determined that more striking results could be obtained by shorter periods of starvation.

The action of semi-starvation on growth and longevity is not limited only to invertebrates. A comprehensive program of study on the role of nutrition and growth in longevity of the rat under the direction of McCay has been in progress for many years and has produced considerable supportive evidence for the relation between growth and aging.

A recent review of these works can be had in McCay's chapter in Cowdry's *Problems of Aging* (22). Some of the key articles are McCay, Crowell, and Maynard (60), McCay, Maynard, Sperling, and Barnes (62), McCay, Ellis, Barnes, Smith, and Sperling (61), McCay, Sperling, and Barnes (63), and Will and McCay (102). Rats were raised on a diet containing all of the essentials but lacking sufficient calories to support growth. In the early experiments rats were maintained on the growth-limiting diet for 766 and 911 days of age at which time an adequate diet was able to initiate growth even at this late date in the life span. Full body size, however, was not reached. The important point is that some of the growth-retarded rats live as much as 200 days longer than the controls.

Robertson, Marsten, and Walters (80) as a result of their experiments on the white mouse concluded that starvation increases longevity. It appears from their data, though, that adequate control procedures were not used and as a consequence their conclusions are not completely justified. Intermittent fasting in the rat tends to increase longevity according to experiments of Carlson and Hoelzel (19). Similar results were obtained by Riesen, Herbst, Walliker, and Elvehjem (78) in their experiments on the effect of restricted caloric intake on longevity of the rat.

Recently, Lansing (51), employing the multicellular aquatic rotifer, obtained evidence which showed that the aging potential does not develop until the time of cessation of growth. Further, it was indicated that rotifers younger than the age at which growth ceases are free of this aging potential. The evidence obtained by Lansing supported the view that aging does not, as commonly believed, begin in the fertilized ovum; on the contrary, aging appears to be a by-product of changes which occur in the cell at the time of growth cessation.

In an attempt to relate calcium changes with age to growth regulation and aging, Lansing (50) proposed that an organic calcium binding complex, probably a protein, located at the cell surface is an integral part of the growth regulatory system of cells. He suggested that changes in this organic complex at the time of growth ces-

sation are directly responsible for the changes which are associated with primary aging.

Experimental Longevity Studies

A number of experimental studies on longevity bear directly on the general physiology of aging. Swerdtfeger (84) analyzed the effect of temperature and starvation on the beetle Melolontha. As has been observed by several other investigators, increase in temperature decreases life span while a decrease in temperature increases life span. Apparently the rate of living is an important factor in determining longevity of the organism. Swerdtfeger also noted that starvation shortens the life span of some beetles while it increases the life span of others.

In a series of carefully executed experiments Jennings and Lynch (39) concluded that the progeny of old parents do not live quite as long as those of young parents. While the observed differences were not statistically significant, the trend in all of the experiments was clear. These studies would seem to indicate that the longevity potential of the individual is conditioned by the age of the parent.

Sonneborn (88) demonstrated the effectiveness of cell multiplication and growth in warding off aging. Using the flatworm, Stenostomum, Sonneborn showed that in vegetative reproduction anterior lines of daughter-animals which undergo little cell multiplication rapidly age and die. Posterior lines, however, whose members must regenerate a large portion of the body, are essentially immortal.

Using a biologic method of measuring physiologic age, Lansing (51) found that aging of the rotifer involves a transmissible, cumulative, and reversible factor. Apparently the ovum is not immune to age changes; on the contrary, it would seem that its physico-chemical organization is altered with age in the individual and that longevity of the individual produced from such an ovum is strongly influenced by this predetermined non-genic factor.

There is a little evidence that the protective action of cell multiplication in warding off senescence can be reproduced experimentally, at least in the protozoa. Hartmann (30) found that Stentor may be reared indefinitely without cell division by means of repeated amputations. Luntz (55) observed that Stylonychia when stimulated electrically undergoes a reduction in size, and cell division is inhibited. He believed that the organism could be rendered immortal by this procedure.

Summary and Conclusions

The view is stressed that the process of aging in living things involves a common underlying series of alterations in protoplasmic constitution. The literature covering the general physiology of aging is reviewed.

Permeability studies with respect to aging seem to indicate that this cell property changes with age and that it may decrease with age. Some studies indicate that the permeability of very old cells reverts to the level found in young cells. The reversion of very old cells to a physiologic state comparable to that of embryonic or very young cells is reported by various workers whose experiments are noted in pertinent sections of the review.

Physical measurements on cells are conspicuous by their non-existence. The few viscosity studies available are insufficient to justify a conclusion. A single report on hydrogen ion changes with age in cells gave negative results.

The literature on organic chemical changes in aging seems to indicate that enzyme activity decreases with age, compounds tending to form insoluble compounds increase with age, and that there is inhibition of the processes involved in protein synthesis. Some theories of aging involving inadequate protein synthesis as a causative factor are considered.

Numerous experiments on calcium changes with age show that this physiologically important cation increases with age. There is evidence relating this increase

with age to changes at the cell surface. Experimental reduction of intracellular calcium increases longevity. Iron tends to increase with age, magnesium decreases with age, potassium tends to increase while sodium gives an inconsistent pattern.

The status of the work on age pigments is evaluated. It seems that more cytochemical work will have to be done on the identification of pigments in standardized material before any general relation between pigment deposition and aging can be determined.

Experiments on a wide variety of organisms indicate that tissue respiration decreases with age. Some experiments support the contention of Child that experimental stimulation of cell multiplication and growth increases the rate of respiration of cells and has a rejuvenating effect.

Nutritional experiments indicate that longevity may be increased by retardation of growth. This has been demonstrated in a number of phylogenetically widely separated organisms. A number of other experiments relating growth regulation to the problem of aging are briefly discussed.

The data that have been reviewed in this article represent but a scratching of the surface of the problem. Aging involves changes in cells of a subtle nature, changes which cannot be detected by direct microscopic observation. Progress in an understanding of the physico-chemical changes in senescent cells will depend upon acquisition of reliable data on specific changes in cells which perhaps ultimately will be blended into a coherent system. We must have data, for example, on permeability, viscosity, hydrogen ion concentration, enzyme activity, and protein synthesis changes with age before much can be done on more than a speculative level.

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CURRENT COMMENT

Progress for Geriatrics

Fifty years ago, the child, the adolescent, the adult, the middle-aged, and the old were regarded by the medical eye merely in the light of chronology.

Gradually it was realized that there were special problems of disease, immunity, nutrition, physiology, and psychology peculiar to the beginning of the life span. Today in this age of specialists there are many pediatricians, many well-established hospitals, many publications, proliferous articles, and numerous syndicated columns devoted exclusively to childhood. This is splendid. As a result, our children are healthier than ever before—and more of them live—to become candidates for critical care at the other end of the span of life.

Slowly we are now beginning to appreciate that the problems of the old are not those of the child, the adult, or even of the middle-aged. The questions of disease, immunity, nutrition, physiology, and psychology still stand, but the answers are different. In the measure that we recognize and understand the differences will progress in geriatrics be made.

Not All Our Egos in One Basket

"A man to make a go of old age must have a variety of accomplishments in which he can take pride." George Lawton and Maxwell Stewart emphasize the necessity for purposeful living in *When You Grow Older*, Publics Affairs Committee, Inc., pamphlet no. 131.

Prefacing the booklet with the dejected picture of a man trained for a single job and forced to retire at a specified age with nothing to do but "hang around," the authors advocate early preparation for retirement by the development of various skills designed to carry over into the age of retirement.

Retirement should not be abrupt, nor should a particular year be automatically the year of retirement for all people. A slight rearrangement of waking hours might be started at forty-five, if feasible, lengthening the number of hours of avocation and rest and shortening those of formal work until at ninety the proportion might be two hours of work, three of avocation, and four of rest.

"As long as we live, some kind of accomplishment is a challenge to us, some problem must be solved. Retirement is not a period chiefly of contemplation. It is one of self-realization, of production."

1868 Mortality Table to be Revised

On January 1, 1948, life insurance companies will abandon the 79-year-old American Experience Table of Mortality and re-

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The hieroglyphics, "The Beginning of the Book for Transforming an Old Man into a Youth," at the top of this editorial page, are from the Edwin Smith Surgical Papyrus, translated by Professor John Breasted, University of Chicago Press.

place it with a new table, the 1941 Commissioners Standard Ordinary Table of Mortality, which bears a more reasonable relationship to the current mortality rate.

Under the old table, children reaching one year of age had a life expectancy of 48.94 years. The new table increases this to 63.76 years.

For persons reaching 20, the old table gave them 42.20 additional years. The new table gives them 46.54 more years.

According to the old table, 98 out of every thousand policy-holders died at he age of 40. According to the new listing, only 62 die.

This new basis for calculating life insurance values provides a more equitable distribution of cost and applies only to policies issued on or after January 1, 1948.

Pilgrim Place in Claremont

Warmed by the sun of Southern California, shaded by palms and tall pines, and with a view of the snow-capped Sierra Madres, Pilgrim Place in Claremont is a pleasant place to spend the years of retirement.

Fifty buildings providing a home for 125 people are located on its twenty-eight acre tract, and many more, including a large assembly hall, are in prospect. There are rooms and suites in the residence halls, apartments in other buildings, and many individual homes which are rented at lower than prevailing rents, the balance of the cost being covered by endowments. It is also possible under a cooperative plan to build a private home on ground furnished on a life-lease basis by Pilgrim Place. The architecture of the various buildings is of the Spanish type with stucco walls, tile roofs, balconies, shuttered windows, fireplaces, and patios.

Each resident is free to live his own life, but there are many planned as well as informal social activities. Space is provided for out-door games and individual gardens, and residents are encouraged to participate in service activities in the Claremont Church and the Red Cross.

Pilgrim Place is intended primarily to serve the families of missionaries, ministers, Y.M.C.A. and Y.W.C.A. secretaries, and other workers in organized Christian enterprises. Its purpose is to enable them to live their own life in their own way within their limited means.

The JOURNAL OF GERONTOLOGY expects to publish an article in an early issue by the Executive Secretary of Pilgrim Place giving details on their methods of procedure and suggestions based on experience gained from thirty-two years of operation.

To Add Life to Years

"Fortify the Forties" says Andrew Allen in *Journal of Living*. He offers six sensible suggestions to get the most out of life after forty:

1) Don't spend any time wishing you were young again.

2) Don't be alarmed if you look older.

3) Don't condemn yourself for past failures.

4) Don't attempt too much.

5) Don't believe that you have reached the limit of your capabilities.

6) Don't be afraid of the future.

To strengthen the Sixties, Dr. Paul Popenoe of the American Institute of Family Relations advises getting out of the rut. "The people who grow old before their time are those who pay no attention to the process or else look upon it as inevitable . . . .

"The great difficulty with many old people is to make them want to get out of the rut. They prefer to stay in it.

"A rut is merely a grave with the ends knocked out. They settle down in it. Pretty soon they are covered with moss; all they lack is a tombstone."

Dr. Popenoe recommends an awareness of the danger and a desire to avoid it. One of the ways of aging successfully, he says, is to make new friends.

Personalized Care for the Aged Client

The *Journal of Social Casework* has compiled a pamphlet consisting of reprints of five articles dealing with the care of the aged which should prove useful to those who are interested in understanding and helping to solve the problems of the elderly.

1) Case Work with the Aged Parent and His Adult Children, by Margaret B. Ryder, is documented by two case histories. One illustrates the problem of a dominating parent and a middle-aged daughter still unable to separate herself emotionally from the person in authority. The other example interprets the difficulties involved when even emotionally mature sons and daughters are confronted with a dominating senile parent. The conflicts brought on by old age, in each case, brought to the surface the deep-seated emotional difficulties established early in childhood.

2. Foster Home Care for the Aged, by Margaret W. Wagner. The elderly who feel the need of close human companionship are those who seek the protection of a foster home where there may be only one boarder but not more than three. The social worker's responsibilities for placing each patient in a suitable home, types of homes, and ways of locating them are discussed and emphasis is placed upon enabling the client to make his own choice to the maximum of his capacity.

3) Boarding Care for the Aged Sick by Sahra S. Rapp. The predicament of the social worker who is confronted with the care of the elderly with long term illnesses is analyzed. The indigent are sent to the municipal hospital, but because of the shortage of medical and nursing staff as well as beds, the case worker finds that other arrangements must soon be made. While there are those who feel that the care of the chronically and acutely ill should be integrated within one hospital, Miss Rapp feels that hospitals devoted exclusively to the care of long term illnesses should be established. Since these cannot be built quickly, to bridge the gap she advocates that:

a) a clearing center be established to give information regarding available nursing home vacancies,

b) an educational program to help the nursing home proprietor be established, and

c) a committee of medical social workers and public welfare workers be established to determine ways and means of making care available to those who are ineligible for Old Age Assistance.

4) A Client Writes the Case Record, and

5) A Client Continues Her Case Record, by Mary Overholt Peters. With a good deal of insight into the client's point of view, the author has created a character, a composite of old age recipients, who in a sprightly way delineates the recipient's response to various types of social workers and her feeling about Old Age Assistance.

Elders in the News

France's oldest woman may be 105 years old, but there is at least one woman older than she in the United States—Mrs. Caterina Repetto, St. Louis, who celebrated her one hundredth birthday in July.

* * *

Kate Johnson of Missouri, 105 years old, worked in a canning factory when she was 75 and walked the three miles to and from work. At 85 she spent her days working in the fields.

* * *

Myron Northey, 101, was amazed to receive a visit from his friend, Charles Bishop, 91, who had walked the entire twenty-five mile distance, and Bishop, who is very careful about his diet, in turn was surprised to find that his friend had lived so long and yet ate whatever he pleased.

* * *

After teaching for more than seventy years, Miss Yula Beatty, 92, is still teaching classes in Alabama.

* * *

George Bernard Shaw, 91 in July, dismissed the occasion with snorts of mock exasperation and the assertion that few others could have survived so much "happy birthday rubbish."

* * *

Seventeen years ago, Ellen Davis, now 94, and William Van Asperen, now 73, met at a square dance. They were married this August.

* * *

Also on the wedding list is John H. Fish, 82, who recently married the woman he saw baptized when she was an infant nearly sixty years ago.

* * *

Ex-Vice-President Dawes observed his eighty-second birthday in August; he is in good health and plans on being at his office daily during the coming year.

* * *

Senator Arthur Capper of Kansas, oldest member of Congress, is learning to fly, at 82, in order to become acquainted with the "basic practical problems" of aviation.

* * *

The title of oldest living pilot is coveted by Starr Nelson, 81, Colorado's oldest member of the Flying Farmers. He began flying in 1941, and since then has owned six planes, has logged more than 700 hours in the air, and has built a fully equipped airport in his hometown of Delta, Colorado.

* * *

A round-the-world flight was recently completed by Mrs. Esther Dower, an 81-year-old resident of Los Angeles. She now plans an airplane trip to Australia.

* * *

A retired farmer, L. J. Michelson, 76, is realizing a boyhood dream. He is making a 1600 mile trip down the Mississippi River from LaCrosse, Wisconsin, to New Orleans, in a 14-foot motorboat.

* * *

Another primitive painter has been discovered. She is a 62-year-old former Navy Nurse, so crippled by arthritis that she can use only two fingers of her left hand. Miss Irene Reid, who has never had an art lesson, learned to paint five years ago by grasping the brush between the thumb and forefinger of her left hand. Each painting takes her about a month to complete.

* * *

A 61-year-old Massachusetts woman says she is growing her fourth set of natural teeth. New teeth grew in as fast as old ones were extracted, she said, until she had a complete third set. A few years ago a dentist extracted four of her third set and now four new teeth are growing to take their place, she has reported. A doctor in England reports in the *British Medical Journal* (no. 4520) that a patient of his, a man aged 82, has just cut a wisdom tooth. And a third set of natural teeth is claimed by Francisco Saiz, Navajo Indian of New Mexico, reputed to be 137 years old.

News and Notes

Division of Gerontology.—Dr. William Kountz and Dr. Esben Kirk are in charge of the new Division of Gerontology established at the Washington University School of Medicine. Laboratories are in the St. Louis Isolation Hospital.

In addition to editorial material placed in this section the JOURNAL OF GERONTOLOGY will accept notices of positions open.

LEGAL ASPECTS

The following are extracts from the bulletins on state legislation, health and welfare, of the Social Security Board. Errors may occur in both bill numbers and titles.

ARIZONA

Excerpts from message of Hon. Sidney P. Osborn, Governor of Arizona, June 9, 1947—". . . You are gathered here to affirm to the people of Arizona that this state has not and will not repudiate its obligation, accepted in the social security laws of 1936, to care for some 30,000 helpless citizens. . . .

"Certainly it will cost money to meet this obligation. If we properly meet it and fulfill the requirements of the social security laws it will cost $14,930,246 for the next two years. . . .

"As Governor of Arizona I cannot submit to you the Social Security Board's request for $12,042,260, which the Board admits will not meet the obligation imposed on the state by law. We cannot in good conscience thus compromise our responsibilities with the obligation to provide decently for those dependents of the state. . . .

" . . . Of this $14,930,246 I am asking you to appropriate, the federal government will contribute about $8,000,000. And when the national government grants that money to Arizona it has a right to insist that the state live up to its own laws for the handling of that money. . . .

"Can you in good faith criticize the administration of our social security programs, particularly before your investigation is completed and the facts put before you? Our administration cost is only 5.3 per cent. That is one of the lowest in the nation. . . .

"This session was called before the regular session's appropriation was found to be unconstitutional in that it would legislate to abolish the merit system set up by law for employees of our social security department, and because all federal funds would be withdrawn without a merit system. . . . "

CONNECTICUT

Aged and Infirm—H. 962. Provides for an appropriation of $600,000 to establish institute for aged and infirm. Passed House June 2. Passed Senate June 3.

FLORIDA

S. 619. Authorizes the State Welfare Board to certify for old age relief certain citizens who meet certain requirements. Introduced May 14 and referred to Welfare Committee.

ILLINOIS

S. 575. Appropriates $2,500,000 for establishment and operation of the Illinois Research Institute for the study and treatment of chronic illness and Geriatrics. Introduced May 26 and referred to Public Welfare Committee.

MICHIGAN

S. 390. Amends section 27 of Act 280 of 1939 as amended by Act 225 of 1945 to reduce amount of property a person may hold which disqualifies him or him and his spouse down to $500 for single persons and $750 for married persons. Introduced May 12 and referred to Public Health and Social Aid Committee.

SOUTH CAROLINA

H. 942. Amends Section 4996-30, Code of Laws of South Carolina, 1942, as amended, relating to old age assistance, so as to provide that such assistance shall be paid to people regardless of their financial condition and shall be at least twenty-five ($25.00) dollars per month. Introduced May 9 and referred to Social Security Committee.

GERONTOLOGIC reviews

FACTORS IN INTELLIGENCE TESTING IN LATER MATURITY

Investigations of intelligence in later maturity have defined several issues which indicate that the field is perhaps more complex than is at first realized. Although several workers (Jones and Conrad, Genetic Psychology Monographs, *13*, 223–298, 1933; Miles, Proceedings National Academy of Science, *17*, 627–633, 1931; Miles and Miles, American Journal of Psychology, *44*, 44–78, 1932; Wechsler, The Measurement of Adult Intelligence, Williams and Wilkins, 1944) have reported upon the distribution of intelligence over a range of ages, a valid interpretation of group and individual measurements on older individuals is still difficult to achieve.

Interpretation of intelligence measurements of older individuals is usually approached from two aspects. (1) present level of intellectual functioning and (2) deterioration from a previous maximal level. Both types of study are made difficult by the lack of large numbers of aged persons available for testing and the lack of representative samples. Data have most frequently been gathered on institutionalized mental patients. Although such studies are not based on the most desirable sampling, they furnish us with some of the best material available in the literature at present.

Work with the Wechsler-Bellevue scale of adult intelligence at the upper age range has been reported by several recent investigators. The Wechsler-Bellevue scale consists of ten short tests. Five of these subtests measure ability to handle ideas and express them verbally and are known as the verbal scale. The remaining five subtests constitute the performance scale, which measures ability to arrive at abstract relationships between groups of concrete objects such as colored blocks which must be arranged to reproduce a pattern.

Separate IQ's may be obtained for verbal, performance, and total scales. On most of the subtests of the verbal scale, the subject is not required to respond within any specific time limit. In most of the performance tests the time required for completion of the response is used in computing the score. Wechsler has assigned weighted scores to the raw scores for each of the ten subtests, such that the mean is ten and the standard deviation is three for all subtests at all ages. Direct comparisons may thus be made among the subtest weighted scores.

Rabin (Journal of General Psychology, *32*, 149–162, 1945) administered the scale to 100 patients between the ages of 60 and 84 at the New Hampshire State Hospital. Only 25 of the subjects were nonpsychotic. He found that the magnitude of the mean scores differed considerably for the senile dementia, cerebral arteriosclerotic, and nonpsychotic groups. The rank order of the weighted scores for performance on the ten subtests, on the other hand, was essentially the same among the three diagnostic categories, with the information and comprehension subtests ranking highest, followed by similarities and digit span.

In general, highest scores were obtained

on verbal and untimed performance subtests. Rabin's results for his total group differ from Wechsler's as to certain of the subtests which do and do not retain their high rank at the older age levels. Rabin finds that capacity for stating the essential similarity between two common objects (similarities) and ability to repeat series of digits forward and backward (digit span) are fairly well preserved, while ability to find important missing details (picture completion) declines. The rank order of these subtests is of significance in the calculation of the deterioration quotient, which indicates the extent to which the individual's level of functioning has diminished from what it was at some previous period of maximal functioning. The deterioration quotient is a ratio between tests which do and do not decline with age, with allowances for normal decline.

Madonick and Solomon (Geriatrics, *2*, 34–40, 1947) gave the Wechsler scale to 50 persons aged 60 to 85 residing in two homes for the aged. As the authors point out, the homes represented selected groups, as is reflected in the occupational distribution. Over half of the subjects are listed as professionals, clerks, and business men; and none of them were unskilled workers. Madonick and Solomon found an order of performance which is, in general, similar to those of Rabin and Wechsler. Of the tests on which Rabin and Wechsler differ, Madonick and Solomon agree with Rabin that similarities remain in third place and that picture completion ranks low. Their results place digits in a rank midway between that of Rabin's over 60 group and Wechsler's oldest complete standardization group (40 to 49).

Rabin points out the weighted score discrepancies between verbal and performance scales in his several diagnostic groups, ranging from 12.8 points for the nonpsychotics to 15.1 points for senile dements. He suggests that such large differences between the two scales have been considered an indicator of inefficiency. We may, however, instead of comparing the weighted scores, make allowance for the amount of deterioration which Wechsler states is normal at a given age by comparing the verbal and performance IQ's calculated by extrapolation for age decline beyond age 60, as indicated by Wechsler (p. 225). The performance IQ of the nonpsychotic group is 104 and the verbal IQ is 102, a difference of only two points. Wechsler states that a variation of eight to ten points between verbal and performance IQ is within the normal range for persons of average intelligence.

The question may be raised as to the validity of using an extrapolation formula. The close approximation to the average IQ of 100 and the small discrepancy between verbal and performance IQ's in Rabin's sample would tend to substantiate Wechsler's formula. On the other hand, Rabin used a small sample whose mean age was only 65.2. Ideally, the IQ ratings for all scores should, as Wechsler admits, be worked out on the basis of a standardization population of sufficiently large number of subjects representative of the older population. This might minimize error introduced by the use of an extrapolation formula based on Wechsler's assumption that the rate of change in IQ after age 35 is practically a straight line. His norms go only to age 59 for the full scale and his curve of adult intelligence differs somewhat from those of Jones and Conrad and of Miles (Kaplan, Mental Disorders in Later Life, Stanford University Press, 1945, p. 72).

The extrapolated full scale IQ for Rabin's nonpsychotic group is 99 (the figure 68.3 mentioned by Madonick and Solomon is the total weighted score, not an IQ). The latter investigators report higher than average mean verbal and performance IQ's of 117.1 and 115.6, respectively, but do not state whether these figures were derived by extrapolation or by using the tables for the highest standardization groups; namely, the 55 to 59 year group for the verbal scale and the 45 to 49 year group for performance.

Assuming that the figures were extra-

polated, we may compare them with the corresponding means obtained by Rabin. Madonick and Solomon reported IQ's of 117 for verbal and 116 for performance scores whereas Rabin found IQ's of 102 for verbal and 104 for performance scales. If the IQ's reported by Madonick and Solomon were not extrapolated, they would be higher after extrapolation, and the difference between their results and those of Rabin would be even greater.

The IQ differences of 12 and 15 points between the two experimental groups may be due to either of the two following factors: (1) the age difference—the mean age of Rabin's group is 65.2 years while that of Madonick and Solomon's group was not reported but from their data it may be estimated at 73 years; and (2) factors of population sampling—the intellectual capacity and educational and socio-economic backgrounds of the residents of private homes for the aged in Madonick and Solomon's study are undoubtedly higher than those of Rabin's state hospital residents.

Recent studies have thus seldom achieved a satisfactory sampling of the population in the years over sixty. Studies of specialized segments of that population, usually chosen because of their availability, do of course add to our knowledge of mental processes in the later years. We therefore have some information concerning intellectual changes in later maturity. The test differences observed in such studies reflect, however, only a particular segment of the increased range of scores characteristic of later maturity. They might lead us to conclude that age changes exist when the differences may actually be a feature of the sampling employed.

In summary, we have reviewed the findings of two investigations using the Wechsler-Bellevue intelligence scale among persons over 60 years of age. Significant problems of interpretation of intelligence in older adults concern differential decline of specific abilities, relative rates of decline of output in the verbal and performance spheres, the influence of speed factors, and the establishment of norms for IQ ratings at the upper age levels. Further studies to clarify these issues should be based on large numbers of persons who constitute a representative sample of the population of the later maturity age range.

CHARLOTTE FOX

CONNECTIVE TISSUE CHANGES WITH AGING

One of the most commonplace observations of aging is that seen in structures composed largely or partly of connective tissue and its components. The skin becomes wrinkled because of loss of elasticity of the underlying dermal connective tissue; chronic degenerative changes are seen in the synovial membranes of joints; bursae become inflamed and calcified; and tendons and ligaments may show inflammation and even calcification. Almost every aged individual is affected in one way or another by connective tissue changes, for they are both more visible and more widespread than changes in other organ systems.

All connective tissues have two fundamental elements in common, the collagen fibers and the amorphous ground substance or, as it is often inaccurately called, the intercellular cement. These two components, and most of the cellular elements which are seen in more highly organized connective tissues, are most easily visualized in the loose connective tissue, which develops from the mesenchyme or middle tissue layer. This layer remains after the other specialized connective tissues have been derived from it in the primitive embryo.

This loose connective tissue is the packing tissue of the body; it surrounds organs, composes the underlying structure of serous membranes and mesenteries and makes up the supporting framework of most other

organ systems. This review will be mainly concerned with the collagen fibers and the ground substance. The collagen fibers are straight, colorless, longitudinally striated collections of closely bound parallel collagen fibrils which are very resistant to stretch. This is illustrated by tendons which are composed almost entirely of closely packed aggregations of the fibers. Wherever collagen fibers are seen, fibroblasts, the cells believed to elaborate the collagen, are also noted.

Sylvia Bensley (Anatomical Record, *60:* 93-100, 1934), who conclusively demonstrated the existence of the ground substance, has shown by histologic methods many important facts of interest in the morphologic aging of connective tissue. She studied the series of changes occurring in connective tissue after loss of the cells following ligation of the pancreatic duct as well as in connective tissue changes in the uterus with the menstrual cycle and the developmental history of the connective tissue of the placenta.

She has shown that young connective tissue is a continuous intercellular, jelly-like substance in which reticular fibers and somewhat sparsely distributed collagen fibers appear and which is remarkably free of tissue spaces. In older connective tissue the sheet-like continuity is lost; tissue spaces and collagen fibers are more prominent and the ground substance or jelly-like material seen in such abundance in younger connective tissue tends to be grouped about the collagen fibers and is apparently reduced.

By proper staining it can be shown that the collagen fibers of older connective tissue are surrounded by denser aggregations of the ground substance than are those of younger connective tissue where the ground substance stains homogeneously throughout the preparation. Therefore the reduction in ground substance noted in older tissues by Bensley may actually only represent a morphologic regrouping and not a true reduction in substance.

It has long been assumed, though never clearly demonstrated, that the aging of the connective tissues is intimately involved with a process of dehydration. Aschoff (Introduction to Cowdry's Arteriosclerosis, The Macmillan Co., 1938), in writing of the aging of connective tissue, stated that " . . . Undoubtedly processes of dehydration play a prominent part and are more or less definitely linked with precipitation." Several groups of workers have recently demonstrated by histochemical methods that in the course of fetal development and normal growth a process of apparent dehydration does occur. This apparent dehydration has been shown, however, to be actually an increase in the ratio of cells to extracellular fluid.

By histochemical methods Lowry and Hastings (Journal of Biological Chemistry, *143:* 271–280, 1942) (Journal of Gerontology, *1:* 345–357, 1946) found that a rise in extracellular fluid occurs in old age contrary to the common assumption. This may, of course, be only a relative increase because of atrophy and decrease in the cellular compartment. Lowry and Hastings (Cowdry, Problems of Ageing 728–747, Williams & Wilkins Co., 1942) conclude that " . . . Actual evidence for change in the composition of the cytoplasm that remains functionally active in the very old individual is still lacking."

As yet no method has been devised to differentiate diffusing extracellular metabolites and their bound water from the water content of the ground substance and the collagen fibers. If this could be done by histochemical electrolyte analysis, or any other method, the problem of whether or not dehydration occurs in aging connective tissue could be conclusively settled. Many chemists believe that a process of dehydration does occur in connective tissues with aging. They state that with aging the colloids of protoplasm condense from a state of fine dispersion to a coarser granular one. This results from the depression of the mutually repelling electric charges of the particles. This depression or loss of electric charge results in coalescence of small parti-

cles into larger ones which tend to fall out of solution.

Some writers state that there is a loss of reactivity in the colloidal systems of protoplasm with aging. Duran-Reynals (Journal of Gerontology, *1:* 358–373, 1946) believes that the age of a tissue is the most important single factor in determining its permeability. He notes that a dye injected intradermally spreads over a much larger area in young than in old subjects and faster spreading of the inoculum of infectious agents is also seen in young tissues. The actual physico-chemical basis for this difference is not definitely determined.

Aside from any changes in hydration that may occur in connective tissues with aging, the changes in the colloid phases and the tissue permeability, special processes of degeneration are seen in structures which are subjected to mechanical stresses. These, in general, are the so-called trophic changes best illustrated in the media of arterial walls. Here atherosis, hyalinosis, and deposition of calcium salts may accompany the changes seen in relatively unspecialized connective tissues. These trophic disturbances, which are not confined to the blood vessels alone, are always preceded by and accompany the changes in the connective tissue elements of the structure in question.

Further investigation into the fundamental physiology and biochemistry of connective tissue is important for more complete understanding of the aging process and to clinical medicine. As noted by Baehr and Pollack (Journal American Medical Association, *134:* 1169–1174, 1947) clinicians have recently been placing increasing emphasis on the collagen degenerative diseases—rheumatic fever, rheumatoid arthritis, periarteritis nodosa, thromboangiitis obliterans, serum sickness, disseminated lupus erythematosis and diffuse scleroderma as a group. Work which might further the correlation of observations on the aging of the colloidal system of protoplasm with the finding of increased hydration in senescence by histochemical methods should be extremely valuable. If such a correlation could be made and used to elucidate the mechanisms of morphologic changes with aging and with the changes of necrosis or fibrinoid degeneration seen in connective tissue diseases, very important practical results would be achieved.

HARRISON F. WARD

GERIATRIC PROBLEMS

OLD AGE IN NEW YORK CITY, Helen Hardy Brunot, Welfare Council of New York City, New York, 1943, 128 pp.

This report is concerned with the problems of old persons and the facilities available for their solution in New York City. Data have been taken from the records of the Bureau for the Aged of the Welfare Council of New York City, which is an information and referral center of the health and social services available to the aged. The information was obtained from old people themselves or from their relatives or friends who sought information on facilities or services for older people. A total of 1,935 case records constitute the source material. Detailed case reports illustrate the kinds of personal problems with which the aged were faced and something of their experiences in trying to obtain assistance from community agencies.

Although financial difficulties represent a major issue in over half of the cases, the prejudices of the community itself against older people contributed heavily to their difficulties. It was found that chronic illness was constantly confused with old age. For example, symptoms of arthritis, arteriosclerosis, heart disease, paralysis, asthma, diabetes, or other chronic disorders in both the middle aged and old, were often regarded as the inevitable manifestations of aging. This confusion was reflected not only by the aged themselves, but also by their relatives, friends, and even by some social workers.

About seven out of eight of the requests for care of persons reported physically ill or disabled asked for the removal of the old person from the inquirer's home. In the majority of these cases, the health factor was described as the dominant problem. Paradoxically, instead of seeking facilities for diagnosis and treatment of the disease, the inquirer was looking for a kindly asylum for the patient during his remaining years. This rejection of the older person by the community both with respect to care and employment is apparently one of the basic problems in gerontology.

According to this study, the type of care needed for the chronically ill patient ranges from the need for actual hospitalization through out-patient clinics to a minimum of personal assistance such as housekeeping aid or even companionship alone. The community has already developed procedures to care for patients who are emotionally disturbed to a point approaching mental illness. However, no provisions for providing appropriate care have been devised for the elderly person who shows signs of only mild mental deterioration characterized by such symptoms as repetitious conversation, tendency to dwell on past events, forgetfulness, and the gradual breaking down of habit patterns. While these people are not able to live alone and need some guidance from others, they do not require the highly specialized facilities of the hospital for the mentally ill.

Financial dependency was a problem in about two-thirds of the old people who came to the Bureau for information. Only 4½ per cent were still employed even though a significant number were able and anxious to work. The constant rebuff which the older worker encounters in the labor market contributes significantly to his psychologic dependence. Although work

tempo may be slowed down and physical strength and endurance reduced, many of these older people possess a potential work capacity that a more imaginative society might well direct into useful work. Both society in general and the individual in particular would benefit by some type of occupational activity.

The use of leisure time is also pictured as a problem of the aged. Not only are many older people ill prepared to use the surplus of leisure which they have, but also most older people need help in finding congenial companionship. They do not make new friends easily, and the community has almost no resources for recreational or social activities for them. A large number of elderly people in the community offers both a challenge and an opportunity to settlement house groups and recreational organizations to extend their programs in the interest of these persons.

The facilities available for meeting these problems of the older population are grossly inadequate. In New York City the population above the age of 65 was approximately one-half million in 1940. In that City the Department of Public Welfare provided monthly cash grants to some 55,000 dependent persons over the age of 65. For group care there were 90 homes for the aged, which together provided living facilities for 12,000 old people. Of these, only two are public homes. One of these public homes on Welfare Island is housed in buildings dating back to 1846.

There are 88 voluntary homes in the area which have a combined population of about 9,000 aged persons. These homes are in most cases supported by special fraternal, church, nationality, or occupational groups and are, therefore, available to the community in only a limited sense because of the stringent admission requirements. In most instances every bed is filled, and application lists are so long that estimated waiting periods vary from one to five years. It is pointed out that financial assistance is not enough. Many of the problems encountered by these older people require varying degree of institutional and public care.

Community facilities needed to meet the problems of care for older people are discussed in some detail. Case workers are still handicapped by their lack of knowledge of changes which characterize normal aging. Consequently, they are often baffled when attempting to plan with a person whose physical and mental powers are diminishing.

Furthermore, the facilities for the care of the aged must be greatly extended. This means not only the development of general hospitals providing long-term, low-cost care for the chronically sick and disabled, but also the development of non-institutional nursing homes. Such facilities would require public supervision and would fill the gap between the patients who require medical and nursing care and those for whom simple custodial care is adequate.

In order to preserve a degree of independence in the older person, some arrangements for supplying housekeeping assistance as part of the budget adjustments would greatly improve the lot of many older persons who require financial aid. Such patients could well receive the needed medical supervision given in outpatient clinics, thus conserving hospital beds and institutional facilities.

The need for development of community recreational facilities for older people appeared repeatedly in the requests for information which came to the Bureau. It was also observed that there is a great need for semi-protected living arrangements that would safeguard and supplement the reduced energies of the old but at the same time permit as much individual choice and freedom as possible.

If the added years of lengthened life span are to become a period of useful activity of health and general well-being, it is obvious that community services will have to go beyond those for simply relieving distress and suffering. Programs of health education, mental hygiene, vocational guidance, occupational retraining, employ-

ment services, and recreation will need to be extended not only for the aged, but for those approaching old age.

While this study presents a somewhat dark picture of available facilities for the care of the aged, it is of major importance to all those concerned with such care. Similar studies in other locales are clearly needed. It serves also to emphasize the need for further research on the physiologic, biochemical, and psychologic characteristics of aging.

N. W. SHOCK.

PHILOSOPHICAL ASPECTS OF AGING

DAS ALTER ALS SCHICKSAL UND ERFÜLLUNG, A. L. Vischer, Benno Schwabe & Co., Basel, 1945, $2.85. (Albert J. Phiebig, American representative, 545 Fifth Ave., New York.)

The author in writing this book has drawn on his experiences and impressions of twenty years spent as physician at the Altersheim of Basel. He offers the reader more of a cultural and philosophic study and less of the clinical than one might expect from a geriatrician.

The book is divided into approximately three equal sections. In the first, Dr. Vischer considers the theory of aging and its characteristic processes, both mental and physical. In the second he deals with the duration of life and touches upon the life span of animals and the literature on rejuvenation and on the prolongation of life by such as dietary means. In the third, he discusses society and the individual in old age, foreign cultures, primitive societies, the battle between the younger and the older generations, and personal orientation towards old age.

The author enjoys a wide acquaintance with the fine arts and the Continental classics. He shows that art offers a means of studying some of the psychic processes of aging, e.g. that comparison of paintings and sculpture created by long-lived artists in their youth and in their advanced age reveals alterations of the artists' interpretations of life and the world.

Most of his literary allusions, which are not familiar to a reader of English, provide interesting illustrations of reactions to aging through the centuries; for instance, quotations from *Discorsi della Vita Sobria*, written by the Venetian nobleman, Lodovico Cornaro (1467–1566) at the age of 83 and translated into many languages.

Written when even the educated believed in the efficacy of the philosopher's stone and potable gold for prolonging youth, Cornaro counselled and practiced moderation, if not semi-starvation, in diet; and his work is adorned with such aphorisms as "Let him who would eat much eat little" and "The food you do not eat is of greater benefit than that which you do." Equally cogent is the comment of his countryman, the playwright Goldoni, three centuries later: "He lived his whole life as an invalid and finally died in good health."

Das Alter als Schicksal und Erfüllung has been translated into Swedish and Hungarian, but the appearance of an Italian translation was delayed because of the war. It is regrettable that it has not been translated into English. While not intended as a text on geriatrics, it does provide philosophical reading in the best sense of the word. We have an analysis of old age written by one who is qualified not only to treat the topic objectively, but who can also sense and discuss humanistically its less tangible aspects.

T. B. ROSENTHAL

BOOKS RECEIVED

Books received since June 1, 1946, are acknowledged in the following list. Insofar as space and time permit, some will be selected for review in a later issue, but it is unlikely that all will be reviewed.

Care and Treatment of the Elderly and Infirm, Report of a Special Committee of the British Medical Association (pamphlet), 1947, 28 pages.

Das Alter als Schicksal und Erfüllung, by A. L. Vischer, Benno Schwabe & Co., Basel (American representative: Albert J. Phiebig, 545 Fifth Avenue, New York), 1945, $2.85, 240 pages. (Reviewed in this issue, page 351.)

Medical Aspects of Growing Old., by A. T. Todd, Williams & Wilkins Co., Baltimore, 1946, $3.50, 164 pages.

Old People, Report of a Survey Committee on the Problems of Ageing and the Care of Old People, Oxford University Press, Oxford, England, 1947, $1.50.

Personalized Care for the Aged Client (pamphlet), Family Service Association of America, New York, 1946, $.50, 24 pages. (See Current Comment, p. 341 this issue.)

Population Index (pamphlet), vol. 13, no. 3, School of Public Affairs, Princeton University and Population Association of America, Inc., 1947, 271 pages.

Treatment of the Patient Past Fifty, by Ernst P. Boas, The Year Book Publishers, Inc., Chicago, 1947, $5.75, 479 pages.

When You Grow Older, Public Affairs Pamphlet no. 131, by George Lawton and Maxwell S. Stewart, New York, 1947, $.20, 30 pages. (See Current Comment, p. 339 this issue.)

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